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Some Observations on the Prevalence of Rheumatic Heart Disease in Canada

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MOST statistics on the prevalence of rheumatic heart disease are far from accurate. They provide a general idea of the frequency of this affliction but no more. If one examines such data, several sources of error make themselves manifest. These are mainly related to difficulties in diagnosis whether due to differences in examiners, varying standards or multiple labels. In spite of these limitations, some interesting figures are available in Canada and a few of the more pertinent ones have been collected and set down here.

In 1940 the medical officers of health in eighteen cities across Canada were good enough to assemble their figures on heart defects among their school children. These are shown in Table I. Under the term *Heart Defects* may be included a variety of abnormalities. It will be noted that the prevalence ranged from 0.4 per cent of the school population to 4.9 per cent. There was some general agreement among the figures, with the average between 1 and 2 per cent. At the same time, certain disagreements were obvious, such as the finding of 3.65 per cent in Oshawa, while in Toronto, only 40 miles away, the prevalence was 1.35 per cent.

In an attempt to arrive at a more accurate estimate, a card was prepared for the use of the school doctors which aided in discriminating between murmurs of functional, congenital, or rheumatic origin. For one year, 1941, these were

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TABLE I

HEART DEFECTS IN SCHOOL CHILDREN
EIGHTEEN CANADIAN CITIES

Medical Officer Reporting	City	No. of Years before 1940	Average No. of Children Examined per year	Average No. of Heart Defects per year	Percentage of Defects in No. Examined
Keeping	Charlottetown, P.E.I.	10	253	12.4	4.9
Cameron	Fredericton, N.B.	10	1727	28	1.62
Gagnon	Montreal, Que.	10	68,410	2230	3.25
Jackson	Toronto, Ont.	12	24,380	329.3	1.35
Crawford	Winnipeg, Man.	1	30,553	143	0.468
	These statistics include:		2347	4	0.170
	6-year-old entrants, 1939;		25,050	118	0.471
	elementary grades, exclusive of 6-year-olds in Grade 1; high school students.		3156	21	0.665
Bolton	Brandon, Man.	6	854	15	1.77
Wilson	Saskatoon, Sask.	10	1689	41	2.4
Hill	Calgary, Alta.	4	1695	18	1.06
Little	Edmonton, Alta.	5	2936	36	1.24
White	Vancouver, B.C.	8	11,105	125	1.12
Anderson	Victoria, B.C.	5	2737	20	0.73
Currey	St. Catharines	1	1469	15	1.02
Wilkey	London	2	2872	43	1.49
	A total of 8,415 health record cards were reviewed. Each child had had at least one medical examination in the past five years. Many had had two medical examinations by the school medical officer, and some, three or more during this time. Percentage of children with definite heart defects recorded.....1.01 Percentage of children with hearts under observations but not recorded as definitely defective 3.39				
Kenner	Stratford	7	718	10.5	1.47
McKay	Oshawa	12	781	28.5	3.65
Fraser	Kitchener	10	1369	9.5	0.7
Davey	Hamilton	16	16,561	137	0.82
	These statistics include public, secondary, and technical schools, and high schools of commerce, as follows:				
	Public School	16	12,932	82	0.63
	Secondary " Technical " Commerce "	14	3609	55	1.5
Hyttenrauch	Windsor	7	10,404	168	1.61

TABLE II

EXAMINATION OF SCHOOL CHILDREN BY THE DEPARTMENT OF PUBLIC HEALTH OF TORONTO
1941-1945

Year	No. of Children Examined in Public Schools	Total No. of Children in Public Schools	No. of Children found to have heart defects non-rheumatic	No. of children found to have heart murmurs, considered rheumatic, in group exam.	Percentage with rheumatic type type of murmur	Computed actual no. of children in public schools with rheumatic heart disease
1941	22,532	85,530	141	204	0.9	775
1942	20,397	84,090	138	119	0.58	490
1943	22,646	82,633	94	119	0.53	435
1944	22,489	83,205	81	108	0.48	400
1945	19,849	77,609	50	81	0.40	315

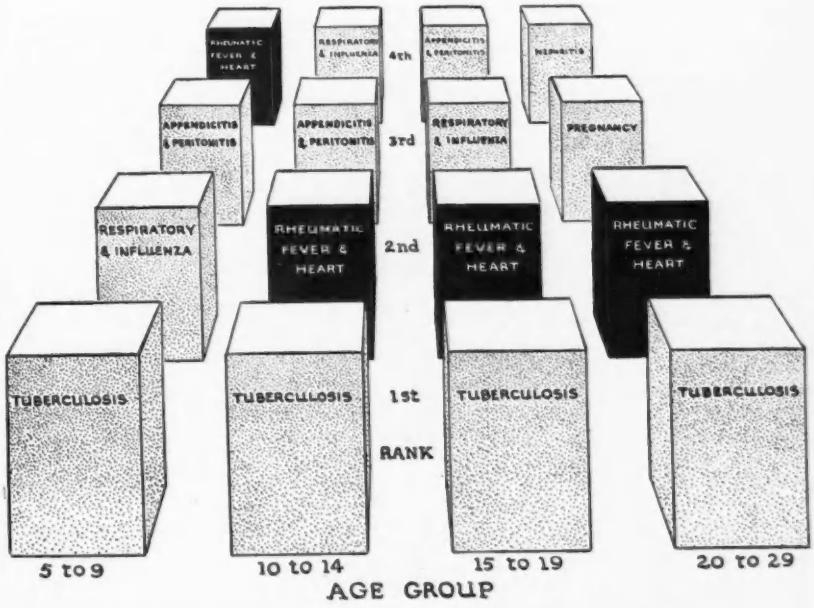
Average age: 9.5 years Range: 6-15 years

filled out in Toronto, Ottawa and Calgary. The percentages that were found to be of the rheumatic type were as follows:

	Percentage of children examined who had rheumatic type of murmur	Percentage of total cardiac defects which were rheumatic
Toronto	0.9	56
Ottawa	0.64	35
Calgary	0.7	50

Approximately half of the cardiac defects found in school children in these three cities were of the rheumatic type. If these cities are representative of the country as a whole, the prevalence of rheumatic heart disease is less than 1 per cent across Canada.

FIGURE I
LEADING FATAL DISEASES, CANADA, 1942

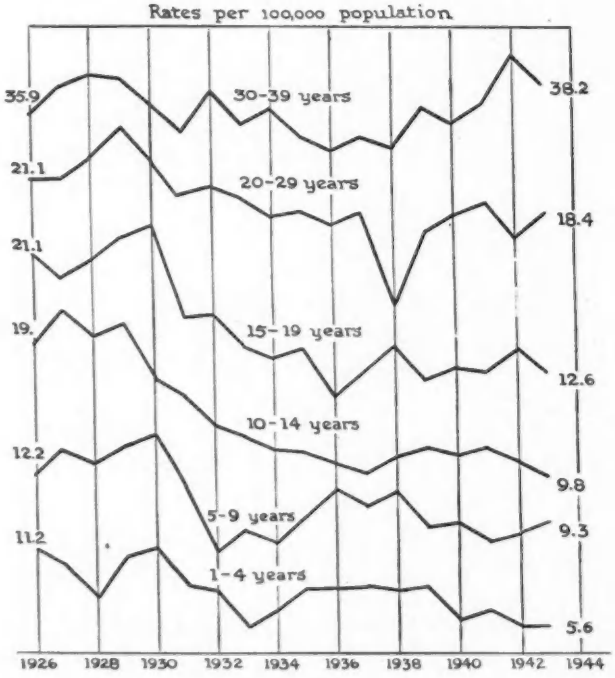


In Toronto this special tabulation card was continued in use up to the present time. The results from 1941 to 1945 are given in Table II. These figures show a decline in the frequency of the rheumatic type of murmur which at first glance might be considered quite significant, but when one notes that at the same time the non-rheumatic defects declined to an even greater degree, a decrease in accuracy of recording is suggested rather than a true reduction in rheumatic heart disease. Changing personnel during the war years, coupled with absence of those particularly interested in those tabulations, probably contributed largely to this apparent decline. It illustrates again the importance of a recording system that maintains a constant method of seeking, diagnosing and registering cases.

Eighty to ninety per cent of school children who die of heart disease are suffering from rheumatic heart disease. Furthermore, the percentage is nearly as high in the young adults of 20 - 29 (70 - 80 per cent). Thus one can very reasonably group the deaths from heart disease in these age groups, with those due to rheumatic fever. When this is done with the mortality statistics for Canada, one can see vividly how important a place rheumatic fever holds among the leading causes of death from disease in children and young adults.

FIGURE II

DEATHS FROM HEART DISEASE IN CANADA,* CHILDREN AND YOUNG ADULTS, 1926-1943



*Deaths include: deaths from all heart disease plus chorea plus acute rheumatic fever.

Figure I indicates that tuberculosis comes first in all groups, and that rheumatic fever is second between 10 and 29 years of age.

The most hopeful feature of the mortality figures is the steady decline that has occurred in recent years. Attention was first drawn to this by Hedley (1), drawing on data from various parts of the United States. The deaths from heart disease and rheumatic fever for Canada are shown in figure II. A remarkable drop in mortality from this cause has occurred between 5 and 20 years of age. This is not so marked between 20 and 29 years, and no decrease is apparent between 30 and 39 years.

Other Data

There are several other sources of rheumatic data which give additional sidelights on the disease. One of these is the excellent summary by Porter (2) of medical examinations at the University of Toronto, published in 1937 and covering the years 1921-37. Out of 9,968 students examined, 104 or 1 per cent were found to have definite evidence of rheumatic heart disease. These figures are of particular value because those cases with evidence of heart disease were checked by Dr. John Oille and Dr. Ross Jamieson.

Another interesting source is provided by the Army examinations during the recent war. In 1944 out of 120,000 men examined 0.35 per cent were listed as having rheumatic heart disease and 0.25 per cent as having endocarditis, chronic and valvular. Since it is likely that both these groups are due to rheumatic fever, the total incidence would be 0.6 per cent.

At the Hospital for Sick Children in Toronto a number of children who have rheumatic heart disease are admitted each year for varying periods of time. The total number of cases so diagnosed for the years 1935-1944 were as follows:

Year	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944
No. of cases of rheumatic heart disease	81	87	92	150	111	114	69	70	40	89

It will be noted that there is considerable variation from year to year but approximately the same number were admitted in 1944 as in 1935—ten years previously.

Comment

Dublin (4) has made an excellent review of the difficulties in attempting to draw scientific conclusions from data gathered on rheumatic fever from mortality and morbidity statistics in government, hospital or clinic files. There are the errors referred to previously from diagnostic difficulties: varying standards, different interpretations of sounds and murmurs, and the use of many alternate diagnostic names. He points out that mortality statistics permit rheumatic deaths to be concealed under other diagnosis. The International List of Causes of Death combines anatomical, etiological and pathological terms that would appear to cause overlapping. An example would be the use of endocarditis as a complete diagnosis in some cases and rheumatic heart disease in others. Revision of this list occurs every ten years, making it difficult to go back in previous decades for comparison. Hedley points out that among deaths in a hospital in Philadelphia in 1932 only 62 per cent of those actually caused by rheumatic heart disease were so recorded.

These errors can only be corrected by widespread interest in the disease and a separate plan of improvement for each source of information. One method attempted was that of compulsory notification. It was tried in California and abandoned as inadequate. It is still being used in Chicago and in the Scandinavian countries. Its value is limited by the fact that many cases are not notified. Furthermore, since the disease is so prone to recurrences, some cases may be notified twice. No system of notification would be of much value unless a registry of names was kept also and continuously checked to prevent duplication.

This brings us to the question of a rheumatic registry. Such a recording system was set up in London, England, before the war as part of a plan to care for these partially crippled children. In June 1938 Bach reported that there were 22,800 children, under the age of 16, on their rheumatic registry. They estimated that this formed 2.6 per cent of that age group. Approximately one-third of this group of children had active or recently active rheumatism.

A rheumatic registry offers several advantages. It could provide good data for judging the prevalence of the disease. It could be used to acquaint the patient or the parents with the numerous facilities already available in a community for the care of this type of child (special schools, special classes, visiting teachers in the homes, occupational therapy, available hospitals, summer camps, convalescent homes, etc., and a list of occupations suitable for those with rheumatic heart disease). General information and methods of prevention of recurrences of the disease would also be useful to the patient and could be disseminated through the registry.

A rheumatic registry would be best established where a relatively close contact could be maintained with the physicians and section of the population concerned. Probably schools offer the most suitable opportunity at present. In order to make a registry successful, certain basic functions must be in operation:

(1) The criteria for diagnosis must be agreed on.

(2) Physicians with some experience in rheumatic heart disease must be available to screen the children.

(3) Diagnostic facilities of a cardiac clinic should be available for these physicians so that the children can be referred to consultants, and those necessary investigations with X-ray, fluoroscope and electrocardiogram can be carried out.

(4) A continuous check must be made in the registry to avoid duplication and keep it up to date.

(5) A follow-up system should be established to determine the prognosis in cases so registered.

Once a rheumatic registry was set up for a city or a province, it could draw on many sources of rheumatic data which would be checked and verified by various means. Information on admissions to hospital for rheumatic fever could be registered as well as deaths. Deaths notified by certificate from all medical sources could be reviewed by the medical officer in charge of the registry. Cardiac clinic cases could be so recorded. Data from schools have already been referred to above, but similar information could be gathered from numerous other institutions, such as universities, children's aid societies, special classes for handicapped children, private schools, convalescent homes and summer camps, etc. Notification of the disease might be usefully considered as part of the scheme, but the registry would form the core and act as a filing system and verification centre for all data. Notification would then become simply another means of discovering a few more cases.

The statistics presented in this paper are open to much criticism and should not be taken as an accurate estimate of the prevalence of rheumatic heart disease. However, they are useful in planning how best to study the problem and for arriving at an evaluation of the facilities required to investigate the morbidity and mortality of this serious disease.

The authors take pleasure in pointing out that much of the data presented was assembled by the efforts of the various City Health Departments across Canada.

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NATIONAL CANCER INSTITUTE OF CANADA

The newly formed National Cancer Institute of Canada is taking applications for the position of Registrar. The Registrar will be responsible for the administrative, secretarial and statistical functions of the Institute through the Executive Director. Applications will be received up to April 10, 1947. Preference will be given to applicants holding the degrees of M.D. and D.P.H. The head office will be situated in Ottawa and duties will begin immediately upon appointment. The salary will be in keeping with the applicant's training and experience.

Anyone interested may apply directly to Dr. A. W. Blair, Chairman of the Interim Committee, Regina Cancer Clinic, Regina; or further information can be obtained from the office of the Canadian Public Health Association.

The Clinical Study of Neurotic Disorders in the Plant

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NEUROTIC illness exists in any industry. The physician who attempts to deal with it requires an understanding of how the symptoms and signs are produced. He needs experience in a method of history-taking and examination to establish a diagnosis which will indicate prognosis and treatment. Treatment of such disorders may lead to a reduction in the duration of neurotic disorders. The plant physician, who usually is a general practitioner with no formal psychiatric training, has the first responsibility for this problem. Procedures he may use to advantage and the difficulties he may meet are described in this article.

1. Neurotic Illness Exists in Any Industry

There are sure to be neurotic disorders among the personnel of any plant of over one hundred people any day it is operating. Whether the plant doctor sees them or not, they will be there, because one hundred workers are not one hundred physical bodies *but* one hundred human beings. Some of these one hundred persons are going to be feeling sick because they have trouble in their life. Since they are human they want certain things and their life is a striving purposefully toward these objectives. When they cannot get what they want, they get upset within themselves. They carry an extra load of thought and feeling when they have these personal troubles and in this state they work less efficiently. Some people can face a great deal of frustration and challenging hostility and remain efficient and feel well. The majority of people, however, at some point early or late in their difficulties begin to find it hard to carry on coolly. Their thinking and their feelings become upset. Their work suffers and they feel unwell. Bodily functions are disturbed and they may come to the doctor for help with their troubles or with the mistaken idea that their physical tissues are diseased.

These neurotic disorders will be found in various guises: absenteeism, fatigue, inefficiency, personality clashes, and changing employment may be presented to the personnel department. Proneness to accident or careless preoccupation may bring them to the first-aid man. Statistics of industrial sickness may show disordered physical states, as "nervous dyspepsia", anaemia, myalgia, or hypotension. Non-specific terms, as "general debility", "nervous exhaustion" or "fatigue state", may cloak them. Where there are frank errors in diagnosis they may be listed as chronic sinusitis, chronic tonsillitis, hyperthyroidism,

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Ménière's disease, or chronic appendicitis. When there is a minor anatomical fault and a major neurotic factor, they may be labelled flat feet, osteoarthritis, or inguinal hernia, etc. The neurotic disorder may prolong a convalescence or complicate a compensation problem.

2. The Production of Neurotic Symptoms and Signs

The physician must clearly command a few simple facts: (*a*) Neuroses are not diseases which exist in tissues but are people who are troubled and feel unwell; (*b*) during the struggle of the person with his environment, physical as well as mental changes may occur as part of his adaptation.

Thinking may be disturbed. Attention and concentration flag and mental fatigue comes on. Loss of interest or a change in interest may arise. The person may develop biases, prejudices, or excuses for his failures. When feelings are disordered, physical changes take place because the emotional life finds its expression in both body and mind together. If a person is in anger, he apprehends this mentally by the angry thoughts that crowd in and by the hostile, aggressive *feeling in himself*. An observer recognizes the man's anger by the flushed face, the distorted expression and the aggressive movements.

These physical components of feeling are conspicuous in states of anger, tension, anxiety and depression. A variety of involuntary changes are effected over autonomic pathways and by hormonal activation. Cerebral circulation can change to produce postural giddiness, syncope and headache. Tinnitus may develop. Nasal vascularity and secretions increase. Anxiety states may simulate hyperthyroidism with an elevated metabolic rate and a tremor. The release of endocrine factors, such as adrenalin, may alter carbohydrate metabolism. Small elevations of fever and loss of weight may be seen. Anorexia, nausea, vomiting, diarrhoea and constipation reflect changes in gastrointestinal motility. Spasm of the pylorus, caecum and sigmoid produces abdominal pain. Air swallowing may be the basis of eructation, tympanites or flatulence. The respiratory irregularity of an anxious person may be seen clearly in a spirometer tracing. Tachycardia and hypertension in the apprehensive patient will subside during an interview as he relaxes. The hypotension of a depression may not persist when the depressive mood is lifted. The medical student during examination demonstrates the urinary frequency of tension states. Menstruation can vary or decrease or cease for a time. Peripheral circulation and skin function alters to produce pallor or blushing or sweating or cold hands and feet.

When we are upset in ourselves, our bodies can ache and be a discomfort. The spasms of hollow viscera in neurotics have to be distinguished from peptic ulcer, subacute appendicitis and sigmoid obstruction. Neurotic pain may also arise from abnormal reception of the sensory impulses in the brain. A surgeon, who was recovering from an abdominal operation, was surprised to find that his own scar sometimes ached. He had previously thought that when his patients said their scars were aching the pain was in their imagination. But he observed that the aching in his own scar was real discomfort which only occurred when he was mentally fatigued. If he could relax after a day of difficult operating, the ache vanished. What he was observing were the bodily sensations which rise

into consciousness when we are mentally tired or emotionally disturbed. When our attention and grip on the outside world flags, our thoughts and feelings and bodily sensations come to the fore. When the emotional disorder is continued, the increase in somatic sensibility may become great. If there is fear that a part is diseased, the upflowing sensory stream from that part will be magnified in consciousness as sensations which are hostile, annoying and irritating. They are discomforts and may be intolerable enough to be interpreted as pain. This is the basis for many headaches, postural backaches, sore feet and praecordial pains that confront a clinician. They vanish when the patient's cares are less and his mind is off his body and himself.

3. The Clinical Method

These common observations form the nucleus of the experience by which the physician understands and diagnoses neurotic illness. The functions of body and mind are never separate. They are always related and influence each other as twin expressions of the person's response to his environment.

This brings us to the clinical method which becomes a three-fold investigation of physical and psychological and social factors. It is done in the consulting room by history-taking and examination. Its component parts are:

(*a*) History of present illness
(*b*) Biography of the patient: (i) Family history
(ii) Personal history
(iii) Past health and illnesses
(iv) Personality development
(*c*) Functional enquiry
(*d*) Present state: (i) Physical examination
(ii) Psychological examination
(iii) Social examination

For example: A patient complains of fatigue. If the body alone is studied, the real trouble may never be found. An expanded study of the total situation may explain the complaint. In the *history of present illness* the physician should study not only the fatigue but the circumstances as it developed: what thoughts, feelings and social stresses were going on at the same time? If this is done, a host of simple relationships may be found to shed light on the physical symptom. The patient was energetic and well until the foreman changed or until his daughter took sick. He can describe his upset feelings and his fatigue developing together. He may describe the loss of appetite, the rising tension, and the preoccupation with the new trouble. He knows he is more irritable and impatient and has lost his sense of humour. The fatigue is variable and is banished by alcohol, cheering news or pleasure.

The history then leads on to the whole *biography of the patient:* his family and his life as a child with them; what they were like, and how they influenced him; how he grew up to hold his adult desires and values and habits; the occupational record in detail. This information may flood one with an understanding of the way this person has learned to struggle for a living. The small variations in health and vigour as well as the past illnesses are important. What concepts of his physical state has he developed from his doctors, his reading or his own conclusions?

The *functional enquiry* must be thorough for each physical symptom, and this is followed by a specific enquiry of the past mental life. Periods of tension, depression or "run-down spells" are correlated to the events in his life which precipitated them. Severer neurotic and mental episodes may have existed and will influence the prognosis.

With the history of the past completed, one turns to the *present state.* A physical examination is a study of the physiological state as well as the anatomical structure. These neurotic processes disturb physical functions so predominantly that the major problems during the examination are in the realm of applied physiology.

A psychological examination is made systematically. Just as inspection is followed by palpation, percussion and auscultation, so is thinking, then feeling, and then behaviour surveyed. This combines the direct observation of behaviour and the analysis of intangible mental processes. To study thinking, the clinician must gauge the patient's attention and memory and reasoning and learning capacities. He must get the patient to reveal the thoughts that chiefly occupy his mind. To study the feelings some clues may come from the patient's expression and behaviour. But, as well, the examiner must be able to talk the language of emotions and lead the patient to describe his own. These inner states may be missed completely if the patient is outwardly phlegmatic and is not led to talk. Such leads as: "How do you feel in your self?", or "How are your spirits?", may get him started. Terms such as "keyed-up", "down in the dumps", "no life in me" may be the crude vehicles he employs to describe those diffuse experiences that are so difficult to express in words.

Finally, the study is concluded by a survey of the present social circumstances. The physician should learn particularly what are the significant stresses for the patient. He may have to enquire from the family at home and from the workmen in the plant to get the data he needs.

Such is the clinical method for the neurotic disorder. It is the same method that is necessary to reach a sound diagnosis and prognosis and a plan of treatment for all other illnesses. There will be a sense of novelty and strangeness only if the physician has never systematically gathered data in the psychological and social fields.

The question should be raised whether this method can be applied in industry by a family physician who lacks formal training in psychological medicine. I am sure it can, provided he weighs the advantages and difficulties of his position. His advantage is that, if he is a good general practitioner, he will have been an apt student of human nature. He will also have a vaster experience of the minor neurotic and emotional disorders that rarely reach a consultant or a hospital. As a family physician he will have the greater knowledge of social stresses in the home, and as industrial physician he will have first-hand knowledge of the plant and the workmen and the work. A last but crucial consideration is that in Canada it would be a severe dislocation in the practice of medicine if the general practitioner did not take the first responsibility for the neuroses. These cases are too numerous, and consultant physicians and psychiatrists will always

be too few to begin to cope with the problem. And a great number of neurotic disorders are not severe enough to require major psychological therapies.

His difficulties will be at least four:

(1) Time and money—A history such as I have outlined requires one to two hours to complete. Treatment will require one-half to one hourly interviews. This must be allowed for in the doctor's day and must be paid for by an adequate fee.

(2) To the plant doctor some workmen will refuse to divulge history they do not wish the firm to know.

(3) Physical diagnostic methods must be exact enough to establish or exclude any significant physical disease. If the physician is in doubt as to his physical findings, he will not be sure of his neurotic factors.

(4) He will have to struggle with the problem of identifying the more serious neurotic and mental disorders which require consultant opinion and specialized treatment. Without formal training he may be baffled by the severe hysterias, the chronic anxiety states, the mild depressions and the obsessional states. Psychotic and prepsychotic states will be less common in industry. Psychopathic personalities and alcoholics will turn up and organic lesion disease will require diagnosis.

Despite these difficulties the general physician should do all he can to manage the neuroses up to the level of diagnosis and treatment he can hold with confidence. He will require consultant services which can be provided by physicians and psychiatrists who have had formal training in treating neurotic disorders. Industry must pay for these services where diagnosis and treatment require extra time.

4. Treatment

Treatment of neurotic disorders will lead to a reduction in the duration of their disability. This may sound dogmatic but many observations support it. Treatment means the management of physical, psychological and social factors where they can be influenced, and treatment means the avoidance of symptomatic treatment and procedures when they are definitely not indicated. To do some good and no harm is the two-edged sword of any therapy.

To return to the physician in the plant who has completed his clinical study: He has analyzed his case findings and judges what can be altered to get that individual person feeling well and contented and strong again. If there are important physical factors such as weight loss or insomnia or associated physical disease, these are treated as such. If the physical symptoms will vanish as the mood lifts, they can be left to take care of themselves. The physician will then get on with the main business of altering the patient's thoughts and feelings. Here the art of medicine is compounded with his scientific analysis of the case. We know the physician's word and manner can heal or ease a troubled mind. By taking time to talk with the patient in the light of the case findings the physician can suggest hope, can explain misconceptions, can allay secret fears and can counsel the man to help himself. The interviews should be one-half to one hour at a time and in privacy, free from interruptions. The guide in this

psychotherapy is the case record. Skill and success come with practice.

It may be possible to lighten social stresses. For this the co-operation of the factory management or the family at home must be obtained. Better recreation and healthy outside interests may be necessary. Working conditions in the plant may be altered with benefit.

The procedures to avoid are equally important. If the problem is the patient's troubled life, it is an unkindness to lead him to believe that his body is diseased. But this may be what he concludes when we prescribe injections, vitamins, tonics, hormones, physiotherapy or sedatives for a neurosis. An unnecessary surgical operation may leave a scar in his mind. To treat a neurosis as a physical disease is to grossly abuse the patient. Such procedures may comfort him for a time but when he again gets upset he is worse than before because he is convinced that at least one doctor found the trouble in his body.

One last point: is this the least expensive way to treat neuroses? It is a difficult question to answer. But when one considers the present bills that neurotics and industry pay in absent time, compensation, hospital care, laboratory investigation, and for doctors and drugs, it might be more economical to pay for a few hours of rational study and early treatment to help the person with his troubles.

Plague, Rocky Mountain Spotted Fever, and Tularaemia Surveys in Canada

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SURVEYS relating to plague, Rocky Mountain spotted fever, and tularaemia were initiated in Canada in 1938 jointly by the Dominion and Provincial Departments of Health. These investigations were given impetus by the occurrence, during the previous year, of what in retrospect appears to have been a human infection and death in Alberta from sylvatic plague. The term "sylvatic plague" is used, perhaps unfortunately, to designate *Pasteurella pestis* infection in wild rodents as differentiated from domestic rats, but differs in no way from the infection in the latter. During the first few years the surveys covered only the southern parts of Alberta and British Columbia, but later were extended to include Southern Saskatchewan. In addition, minor surveys have been made at the ports of Halifax, Nova Scotia and Saint John, New Brunswick, and in 1943 intensive surveys were carried out by army personnel in the areas adjoining army camps in the three Prairie Provinces.

In Alberta and Saskatchewan the surveys are conducted only during the summer months—roughly from May to September—embracing the period of tick and ground squirrel activity. Prior to 1943 the British Columbia field crews were employed for similar periods on tick and ground squirrel surveys in the interior of the province, and during the autumn months on rat surveys at the ports of Vancouver and New Westminster.

In 1943, following the appearance of plague infection in rats at Tacoma, in the adjoining state of Washington, rat surveys in British Columbia were extended to all the deep-sea ports and adjacent municipalities in the province on a year-round basis, and interior surveys were left in abeyance.

The methods of obtaining specimens are in effect the same as indicated by Gibbons (1, 2) and Gibbons and Humphreys (3).

PLAGUE

Collections of the various rodents encountered—ground squirrels, rats, and mice—are made by trapping or shooting. Each rodent is immediately placed in a paper bag to insure retention of its ectoparasites. The parasites are then stupefied with choloform and collected into vials of 2 per cent saline. The rodents—with the exception of mice—are dissected in the field and any suspicious lesions disclosed are removed. These together with the ectoparasites are shipped in iced containers to the laboratory for animal inoculation. During the first few years of the survey it was customary to rely on the post-mortem

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findings; if no lesions resembling plague were discovered, no tissue specimens were taken. But of recent years, especially on the rat surveys, when no evidence of infection is found, a tissue pool is taken from five or more of the animals of each day's collection and submitted to the laboratory as a check for possible latent infections. At the laboratory the tissues are macerated in a mortar with alundum or in a waring blendor. A small portion of the macerated tissue is applied to the scarified skin of one guinea pig, and the remainder, if the specimen is in good condition, is suspended in saline solution, filtered through gauze, and injected subcutaneously into a second guinea pig. Subcutaneous injection seems preferable to scarification, but frequently tissues, especially those from rats, shipped from a distance are toxic and fatal to the guinea pig when injected subcutaneously.

Fleas are submitted in lots of up to 100 and as a rule each lot is counted as one specimen. Each lot is ground in a mortar, suspended in saline, and injected into a guinea pig. If *P. pestis* is present, the guinea pig usually sickens and dies in four to six days, showing the characteristic lesions of plague. At necropsy the infection is passaged to a second guinea pig and to one or two white rats (white rats being highly susceptible to *P. pestis*, but only slightly so to *Pasteurella pseudotuberculosis rodentium*) as an aid in identifying the infection and maintaining it until cultures are obtained. Cultures may be started from the spleen of the first guinea pig, but usually it seems more satisfactory to

TABLE I

SPECIMENS EXAMINED FOR PLAGUE INFECTION
APRIL 1, 1939 TO SEPTEMBER 30, 1946

Province	Type of Rodent	Number Examined				Number Positive	
		Rodents	Fleas	Flea Specimens	Tissue Specimens	Flea	Tissue
British Columbia	Ground Squirrels	7824	18872	365	5		
	Rats	17753	13007	1195	1633		
	Mice	183			99		
Alberta	Ground Squirrels	12676	25411	939	817	32	6
	Rats	2			2		
	Mice	212	8	2	18		
Saskatchewan	Ground Squirrels	7448	36958	356	127	2	
	Rats	435	83	15	17		
	Mice	5	16	2			
Manitoba	Ground Squirrels	698	919	20	26		
	Rats	12	10	5	5		
	Mice						
Nova Scotia (Halifax)	Rats	84	210	40			
New Brunswick (Saint John)	Rats	6	16	3			
Totals		47338	95510	2942	2749	34	6

delay culturing until the second pig comes down. The lesions then are more pronounced and pure cultures are more readily obtained.

A summary of the findings recorded since the inception of the survey is shown in Table I. British Columbia so far has been free of plague infection. In Alberta *P. pestis* was discovered in ground squirrels each year from 1939 to 1942 inclusive, and again in 1945; six tissue and thirty-two flea specimens proved positive. The known infected area now comprises several thousand square miles in the south-eastern part of the province. In Saskatchewan the infection was discovered in Richardson ground squirrels this year (1946) for the first time in territory adjacent to the infected area of Alberta. Two large pools of fleas taken from sixty-one ground squirrels proved positive.

The species of rat fleas collected was determined for each area in order to record the "cheopis index". In the Vancouver-New Westminster area the cheopis species (*Xenopsylla cheopis*) has proved fairly abundant—giving an index of approximately 0.69—but in other cities on the British Columbia coast this species seems to be non-existent. The vast majority, about 95 per cent, of the rats encountered were of the Norway species (*Rattus norvegicus*). Of the remainder, 4 per cent were black rats (*Rattus rattus rattus*) and 1 per cent Alexandrines (*Rattus rattus alexandrinus*).

Black and Alexandrine rats are found most frequently in the water-front areas and it is, as a rule, one or the other of these species that is recovered from ships after fumigation. Curiously enough though, the black rat is found at Nelson, British Columbia, some 500 miles from the sea coast.

Mice are submitted in entirety and dissected in the laboratory. So far we have failed to find any evidence of plague infection in this rodent.

Rocky Mountain Spotted Fever

The aetiological agent of Rocky Mountain spotted fever (*Rickettsia dermacentroxenus*) is transmitted by several species of ticks which serve as its natural host and in which it behaves as a harmless parasite. Its occurrence in the human subject may be regarded as purely accidental, for man plays no part in the perpetuation or host-to-host transmission of the infection.

Susceptible mammals—small rodents, rabbits, and certain other animals—acquire the infection from infected ticks and may in turn, during their infectious period, pass it on to non-infected ticks. In this way the infection is disseminated among the tick population. In the tick the rickettsiae survive for long periods and are aided in perpetuation by hereditary transmission from the immature stages to the adult and from the adult through the eggs to a percentage of the larvae of the next generation. As far as we know, the infection in nature is transmitted only through the medium of a tick.

Three of the ticks known to occur in Canada are proved vectors of spotted fever infection. They are—(1) the Rocky Mountain wood tick (*Dermacentor andersoni*), which is abundant in the southern part of the three western provinces from the Coast Range to some distance east of Regina; (2) the American dog tick (*Dermacentor variabilis*), found in south-eastern Saskatchewan, Manitoba,

and certain parts of Eastern Canada; and (3) the rabbit tick (*Haemaphysalis leporis-palustris*), which is widely distributed throughout Canada, but occurs only on rabbits and certain ground-frequenting birds. It rarely attacks man. The rabbit is peculiar in that, when infected, it carries consistently a very mild strain of rickettsiae. Its role in the maintenance and perpetuation of the infection in nature is not clearly understood, but it is suggested that this tick may provide a source from which virulent strains of *R. dermacentroxenus* arise.

D. andersoni is, at the moment, the only tick in Canada known to be harbouring virulent strains of spotted fever rickettsiae. Evidence of infection in this tick has been found in both British Columbia and Alberta. So far ticks submitted from south-western Saskatchewan have proved negative, although a few suspected cases of spotted fever have been reported from that area.

Rickettsiae carried by a drag tick (i.e., a flat or unfed tick) are rarely infectious until the tick has attached to a host and fed for six to eight hours or more. This lag in infectivity, or the so-called "reactivation period" (4), usually permits the detection and removal of a tick before infection has taken place, and thus the potential number of spotted fever cases is greatly reduced. The fact that reactivation is required, however, adds considerably to the volume of work entailed in the laboratory examination of ticks, for in order to determine with any reliability whether or not a tick is infective it must first be fed.

From twenty-five to thirty ticks are placed on a guinea pig by means of an adhesive-tape applicator, and allowed to feed for three to four days. (For a tick to engorge completely requires eight to ten days.) They are then removed and stored in merthiolate solution (1:1000) overnight to reduce surface contaminants. The following morning they are rinsed free of merthiolate, and ground with alundum in saline for injection, intraperitoneally, into one or more guinea pigs.

The entire procedure is laborious and entails the taking of temperatures on both the host and the injected guinea pigs each day for two or more weeks. If in this time definite infections have not developed, the guinea pigs are given an immunity test by injecting each one with 2 or 3 cc. of fresh blood taken from actively infected guinea pigs. A group of normal guinea pigs are injected at the same time as controls and, as in the original test, temperatures are taken daily for another two weeks. Guinea pigs withstanding the challenge inoculation are given a second larger injection as a verifying test of their immunity. Not infrequently animals which escape infection from the first inoculation succumb to the second.

Evidence of rickettsial infection was obtained from five lots of ticks collected in British Columbia, and from ten taken in Alberta. (Table II.)

In our experience the results obtained in the examination of ticks have been rather difficult to interpret. Frank infections in the test animals have rarely been induced. Positive immunity tests, suggesting the existence of low-grade immunizing strains of rickettsiae, have been observed more frequently, but have always left some doubt as to whether they were authentic. In considering them one is invariably faced with the fact that a certain percentage of the control animals used in the test also showed immunity. Contrariwise, it is somewhat disconcerting to find that on occasion this suggestive evidence of infection is all

TABLE II

TICKS EXAMINED FOR ROCKY MOUNTAIN SPOTTED FEVER INFECTION

Year	British Columbia		Alberta		Saskatchewan	
	No. Ticks Examined	No. Specimens Positive	No. Ticks Examined	No. Specimens Positive	No. Ticks Examined	No. Specimens Positive
1939	10655	1	12417	5		
1940	20767	3	11109	2		
1941	14957	1	13231	1		
1942	25826		5922			
1943			1426		764	
1944			1105	1†		
1945	22*		1765	1		
1946			2226		1243	
Totals....	72227	5	49201	10	2007	

†Plus one isolation from human blood.
*Species unknown.

that can be deduced from ticks submitted from an area where active human infections are occurring. In one instance we were able to confirm the physician's diagnosis of spotted fever by isolating rickettsiae from the blood of a patient—one in whom the infection terminated fatally two days later—but the only indication of infection obtained from ticks submitted from the actual section on which the patient was believed to have been infected was that of a low-grade immunizing strain. It is of interest, however, that the strain recovered from the patient was relatively low in virulence for guinea pigs. At first it induced fever and

TABLE III

Pasteurella tularensis IN SPECIMENS SUBMITTED FOR PLAGUE AND ROCKY MOUNTAIN SPOTTED FEVER EXAMINATION, APRIL 1, 1939 TO SEPTEMBER 30, 1946

Province	Host	No. of times *P. tularensis* Encountered
British Columbia	Wood ticks (*D. andersoni*)	6
	House mouse tissues (*Mus musculus*)	1
Alberta	Wood Ticks (*D. andersoni*)	16
	Rabbit Ticks (*Haemaphysalis leporis-palustris*)	1
	Ground squirrel tissues (*C. richardsonii*)	6
	Ground squirrel blood (*C. richardsonii*)	1
	Meadow mouse tissues (*Microtus sp.*)	2
	Deer mouse tissues (*Peromyscus m. borealis*)	1
	Rabbit tissues (sp. unknown)	1
	Bird tissues (Franklin gull—*Larus pipixcan*)	1
Saskatchewan	Dog Ticks (*D. variabilis*)	2
Total		38

characteristic lesions, but in contrast to the Montana strains, which we have employed and which usually kill 80 to 90 per cent of the test guinea pigs, this strain failed to kill a single animal. It gradually lost virulence with each successive passage until, in about six months, it became quite innocuous and could no longer be maintained.

Tularaemia

The finding of tularaemia is incidental in the search for plague and spotted fever, but since *Pasteurella tularensis* is extremely infectious and insidious, it must be kept in mind and constantly guarded against when dealing with either of the other infections. It appears to be widespread in the Western Provinces and in the course of these surveys has been encountered some thirty-eight times, as indicated in Table III.

Recently the infection was recovered from a house mouse (*Mus musculus*) taken in the Coast Area of British Columbia, where no previous record of the disease has been reported, and it is of interest that this appears to be the first time spontaneous infection in the house mouse has been recorded on this continent. The micro-organism isolated was highly virulent for white mice, but relatively low in virulence for guinea pigs. Culturally and serologically it was quite atypical until it had been passaged several times from mice to guinea pigs.

Discussion

The surveys of the past eight years indicate that plague is well established in ground squirrels in south-eastern Alberta and that the infection has at least gained a foothold in the adjoining territory of Saskatchewan. The findings suggest the possibility of a difficult plague problem in the Western Provinces. Plague in any class of rodent provides a focus from which outbreaks may insidiously occur at any time. As long as the infection is confined to ground squirrels the risk is perhaps not great, for these animals do not frequent dwellings or otherwise come into close contact with the human family. But if rats invade the area and the infection becomes established in them, the hazards involved are obvious.

In pioneer days rats were unknown on the Prairies, and just when they invaded those parts is not certain. Their appearance in Winnipeg was recorded, apparently for the first time, in 1910 (5) and by 1912 they had reached south-eastern Saskatchewan (6). Now they seem to be well established in all the larger municipalities of both Manitoba and Saskatchewan. As yet they do not appear to have colonized in Alberta, although the odd specimen has been taken there—two having been submitted to the laboratory from Calgary within the last two years. On the West Coast of British Columbia rats have been prevalent since the earliest times, and they are found at Revelstoke and Nelson in the interior of the Province. For some unknown reason they have failed to colonize in the Okanagan and other dry belt areas east of the Coast Range.

Rocky Mountain spotted fever is a potential hazard in any tick-infested area. The small number of infected ticks encountered in these surveys would suggest that the infection is not widespread in Western Canada, but the phenomenal œcology of *D. andersoni* and *D. variabilis* provides such unusual opportunities

for dissemination of the infectious agent that every tick must be viewed as potentially infective. Failure to recover the infectious agent from ticks by laboratory examination should not be accepted as a reliable indication that the area from which the ticks were submitted is free of infection. It is possible that strains of rickettsiae which are capable of inducing only mild and inapparent infections in guinea pigs may be highly pathogenic for human beings.

The repeated finding of *P. tularensis* in specimens submitted from widely separated areas is indicative of the wide distribution of this infection, and the ease with which it may be transmitted either by ticks and certain biting insects, or through contact with infected animals, makes it a disease of some concern. In the transmission of the infection from ticks there is no indication that a period of reactivation is required as is the case with the rickettsiae, and no satisfactory vaccine against it is available. Fortunately, however, for victims of the infection, streptomycin is reported (7) to offer marked relief.

Summary

1. A report on the findings of eight years of survey in connection with plague, Rocky Mountain spotted fever, and tularaemia in Western Canada is presented.

2. Plague infection (*P. pestis*) is prevalent in ground squirrels in a large area of south-eastern Alberta and in the adjoining territory of Saskatchewan. Six of 817 tissue pools and thirty-two of 939 flea pools submitted from 12,676 ground squirrels collected in Alberta, and two of 356 flea pools obtained from 7448 ground squirrels in Saskatchewan proved positive.

3. The infectious agent of Rocky Mountain spotted fever (*R. dermacentroxenus*) occurs in ticks in both British Columbia and Alberta. Evidence of the infection was found in five specimens out of a total of 72,227 ticks collected in British Columbia, and in ten out of 49,201 collected in Alberta.

4. *P. tularensis* was encountered a total of thirty-eight times in the examination of specimens—ground squirrels, rabbits, mice, certain birds, and ticks—submitted from various localities for evidence of plague and Rocky Mountain spotted fever.

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A Study of the Diphtheria Antitoxin Response to Recall Doses of Specific Antigen

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THERE is universal agreement that maintenance of antitoxic immunity to diphtheria requires the administration of recall doses of toxoid at periodic intervals. There is, however, a lack of precise information as to what the optimal amount of antigen for the recall dose should be and at what intervals it should be given. In arriving at a decision on these points a number of factors must be considered, the most important of which are the consistency, degree and duration of antitoxin response. In addition, and administratively important, the problem of reactions cannot be disregarded. The observations set out below were made with a view to some clarification of these matters.

Procedure

Various groups, both large and small, of children and adults have served as study material over a number of years. In most cases the previous history of immunization was ascertained. Preliminary blood samples were obtained before administration of the stimulating dose of antigen (detailed below) and further blood samples were obtained at suitable intervals (1) thereafter. Titrations for the antitoxin content of the sera were made by the Fraser modification of the Römer test (2).

Experimental

Groups I, II, III and IV

The first test concerns 50 children ranging in age from 7 to 14 years who had received a primary course of 3 doses of fluid toxoid six years previously. These children were living in a low diphtheria environment so that natural stimuli must have been minimal and no artificial stimuli were given in the intervening period. The children were divided into four groups; 9 were given the Schick test only (0.001 Lf); 7 were given the Schick control only (diluted diphtheria toxoid containing 0.02 Lf); 11 were given the Schick test and control (0.021 Lf); 23 were given 0.1 cc. of fluid toxoid (4 Lf) subcutaneously. Blood samples were obtained five weeks later and again at the end of three years. The results of antitoxin titrations are shown in Table I.

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TABLE I

AVERAGE ANTITOXIN UNITAGE 6 YEARS AFTER PRIMARY COURSE OF 3 DOSES OF FLUID TOXOID AND 5 WEEKS AND 3 YEARS AFTER VARIOUS RECALL DOSES

Group	No. in Group	Antigen	Lf	Average Antitoxin Unitage at		
				0	5 weeks	3 years
I	9	Schick Toxin	0.001	0.007	0.071	0.022
II	7	Schick Control	0.02	0.007	0.35	0.041
III	11	Schick Toxin and Control	0.021	0.003	0.318	0.036
IV	23	0.1 cc. Fluid Toxoid	4	0.007	1.7	0.49

In these 4 groups of children, closely comparable except in point of numbers, the average antitoxin unitage before the recall dose is fortunately almost identical. The responses, therefore, are possibly subject to some direct comparison in spite of the small numbers in the groups.

The pattern is unmistakable. Increasing strengths of antigen evoke greater production of antitoxin as would be expected within certain limits. The antitoxin production is not, however, in direct proportion to the strength of antigen given. The differences between the average antitoxin titres are found to be statistically significant.

It seems rather remarkable that as little as 0.001 Lf of diphtheria toxin (Group I) should effect the recall of antitoxin shown and elicit an increase in 8 of 9 subjects. Toxoid of similar Lf value might, of course, have been less effective. In Group II the diluted toxoid of the Schick control containing 0.02 Lf proved still more effective. It would appear, therefore, that the antigenic effect of the Schick test and control as shown in Group III is mainly due to the latter element. The antitoxin response to these minute amounts of antigen serves to strengthen the possibility that small doses of toxoid should suffice for "booster" purposes. This is borne out by Group IV. Good as the above results are, those obtained with 0.1 cc. of fluid toxoid containing 4 Lf are much more satisfactory. Whereas before this recall dose none had as much as 0.1 unit of antitoxin, five weeks later 100 per cent were at this level or greater, and the average unitage was 1.7.

The loss of antitoxin over a three-year period was appreciable but not greatly different for the 4 groups. It is apparent, therefore, that maintenance of strongly protective antitoxin levels over any protracted period of time is dependent, in general, on the development of high titres to the recall dose. The average antitoxin level of 0.49 units in Group IV at the end of three years is encouraging in this respect.

While the antitoxin titres of these children were not determined following the primary course of immunization, the levels six years later indicate a definite

loss of antitoxin over this period. Thus 6 per cent had less than 0.001 unit and 32 per cent less than the Schick test level of 0.004 unit.

*Groups V and VI**

The antigenic effect of the Schick test and control has been determined over a period of several years in many groups of graduate students ranging in age from 25 to 50 years. In addition to differing in age from Group III considered above, a few had had no known diphtheria experience while some had been immunized very recently and others many years previously. The results in two such groups are discussed and those of Group V are presented in Table II.

TABLE II

DIPHTHERIA ANTITOXIN TITRES BEFORE AND 10 DAYS AFTER THE SCHICK TEST AND CONTROL (0.021 Lf)

Time	0.001 & >	0.01 & >	0.1 & >	1 & >	5 & >	10 & >	20 & >	40 & >	Total	Average Unitage
0	26	21	9	4	2	–	–	–	28	0.64
	93	75	32	14	7.1	–	–	–	100%	
10 days	26	25	20	10	4	1	1	–	28	2.6
	93	89	71	36	14	3.6	3.6	–	100%	

The Schick test and control in this adult group (Table II) served to raise the average antitoxin titre from the rather high preliminary level of 0.64 units to 2.5 units ten days later in spite of the fact that 5 of the individuals failed to respond within the limits of the test employed. Among these failures, 2 possessed < 0.001 unit of antitoxin to begin with, while the other 3 had appreciable amounts. Two of the latter had received toxoid within recent months, which may have altered their ability to respond. Persons without a previous diphtheria experience would, of course, not be expected to respond, but that others may fail to do so for known or unknown reasons is illustrated here.

The results in Group VI differed little from those shown in Table II. The rise in average antitoxin titre was not marked—from 0.71 to 1.73 units. On first bleeding, 6 persons possessed < 0.001 unit and none of these showed a response. All 6 were without a history of previous immunization. An additional 14 who possessed variable amounts of antitoxin prior to the Schick test and control failed to respond within the limits of the first test applied. The sera of these persons were retested using 2-fold dilutions and it was found that 9 showed a slight increase in antitoxin and 5 no increase. Thus, of the 27 in the group with evidence of a previous diphtheria experience, 5 or 18.5 per cent failed to respond to this small stimulus. In addition, 9 of the 27 or 33.3 per cent responded in slight measure only.

Group VII

The 35 individuals of this group were undergraduate university students who had had 3 doses of fluid toxoid from 10 to 18 years previously. At the time that blood samples were taken 0.1 cc. of fluid toxoid (4 Lf) was ad-

**Group VI introduced since publication of abstract (this Journal, 1947, 38: 70).*

ministered subcutaneously to each. Second blood samples were obtained five weeks later. Table III records the results of the antitoxin titrations.

TABLE III

ANTITOXIN TITRES 10 TO 18 YEARS AFTER PRIMARY COURSE OF 3 DOSES OF FLUID TOXOID AND 5 WEEKS AFTER A RECALL DOSE OF 0.1 CC. (4 LF) OF FLUID TOXOID

Time	0.001 & >	0.004 & >	0.01 & >	0.1 & >	1 & >	10 & >	40 & >	>40 <80	Total	Average Titre in Units
0	24	19	14	5	–	–	–	–	35	0.025
	69	54	40	14	–	–	–	–	100%	
5 weeks	35	35	34	33	29	13	3	2	35	9.8
	100	100	97	94	83	37	8.6	5.7	100%	

The loss of antitoxin in this group over the prolonged period since primary immunization is very marked. It is apparent from Table III that 11 or 31.4 per cent possessed < 0.001 unit and an additional 5 or 14.3 per cent had < 0.004 unit. In other words, approximately 46 per cent had become Schick-positive and one-third had no measurable antitoxin. None of these 35 individuals had had a reinforcing dose of toxoid but their exposure to diphtheria bacilli is, of course, not known. However, because of their economic status and the fact that diphtheria cases and carriers have both shown a great reduction over the past fifteen years in this locality, natural stimuli must have been minimal. This is borne out by the antitoxin loss indicated above.

The antitoxin titres five weeks after the administration of 0.1 cc. of fluid toxoid containing 4 Lf are in striking conrtast to the initial titres. All individuals responded to the Schick test level, 0.004 unit, or beyond, and 83 per cent possessed 1.0 unit or more where none was at this level before. The average antitoxin titre rose from 0.025 to 9.8 units.

Group VIII

The effect of 0.1 cc. (4 Lf) of fluid toxoid in stimulating antitoxin response was further tested on a school group of 51 individuals ranging in age from 5 to 22 years, the majority being in their early teens. These persons had been immunized four to twelve years previously, in most cases six years.

The results obtained in this group were very similar to those of Group VII shown in Table III. More persons possessed antitoxin in greater degree, i.e., only 4 per cent had < 0.001 and 8 per cent < 0.004 unit before the recall dose. The antitoxin response was very marked, all showing an increase and the average titre rising from 0.65 to 6.5 units. After the recall dose 90 per cent had 0.1 unit or greater, in contrast to 26 per cent before. On retesting 7 members of this group three years later, 3 were found to have the same titre as before while 4 had definitely lower titres. The average antitoxin unitage for the 7 had fallen from 2.0 to 0.3 unit.

Group IX

A group of 102 medical students was studied in the following manner: on the first day blood was drawn, the Schick test and control performed, and 0.5 cc. diluted fluid toxoid containing 2 Lf was given. Three days later the skin tests were read and reactions to the subcutaneous toxoid noted. Further blood samples were obtained at the end of three weeks. The antitoxin status of these young adults before and after this secondary stimulus is shown in Table IV.

TABLE IV

ANTITOXIN TITRES BEFORE AND 3 WEEKS AFTER A RECALL DOSE OF 2 Lf OF FLUID TOXOID

Time	0.001 & >	0.01 & >	0.1 & >	1 & >	5 & >	10 & >	20 & >	40 & >	Total	Average Antitoxin Titre
0	68	52	23	4	–	–	–	–	102	0.15 units
	67	51	23	3.9	–	–	–	–	100%	
3 weeks	94	87	46	42	13	6	2	–	102	2.6 units
	92	85	45	41	12	5.9	2.0	–	100%	

While the immunization history of these individuals was not obtained, the fact that 68 of the group possessed $>$ 0.001 unit of antitoxin on the first bleeding and that 26 of the 34 with $<$ 0.001 unit responded to this single injection, shows clearly that some 92.2 per cent had had a previous diphtheria experience. There were, then, 8 individuals with $<$ 0.001 unit who failed to respond and one might conclude that the majority of these were without previous immunity. However, 6 others with antitoxin titres ranging from $>$ 0.01 to 1 unit also failed to respond within the limits of the tests applied. If these are actual failures, the explanation is not clear. Previous recent stimulation, as noted in one of the above groups, might account for this finding. In all, then, 14, or 13.7 per cent, failed to respond, but of those with clear evidence of an ability to respond, 93.6 per cent did so.

The increase in antitoxin is again notable as shown by an average antitoxin titre before and after of 0.15 and 2.6 units respectively and a change from 4 to 41 per cent of persons with 1 unit or more.

Reactions to this recall dose were reported by 16 persons or 15.7 per cent. These were mostly slight and local, although 2 manifested some general as well as local reactions requiring brief bed rest, but were not severe. Fourteen of these 16 reactors, including the 2 bed cases, were positive to the Schick test control. There were 3 persons with positive skin test reactions who reported no reaction to the subcutaneous antigen.

While 5 of the 16 reactors showed either no or slight antitoxin increase, all of this group either already possessed or subsequently achieved reasonably high titres. Thus the average titre for these 16 on the second bleeding was 5.6 units as contrasted to 0.52 unit for the other 86, or 2.6 units for the complete group of 102. While the presence of reactors apparently accounts for, in some part, the satisfactory level of antitoxin achieved by the total group, a similar condition would obtain in any older age group undergoing re-immunization.

Groups X and XI

The purpose of this last experiment was to compare the effect of 3 and 40 Lf of toxoid as recall doses. The subjects studied consisted of school children ranging in age from 5 to 17 years. All had been immunized from one to ten years previously. A few had had a booster dose in addition to the primary injections. Blood was obtained from each person and the intradermal reaction test given. The reaction tests were read the following day and the children separated, alternatively, into two groups with the exception of those, 13 in number, with a positive skin reaction test, all but 1 of whom were placed in the first group. The members of this group then received 1 cc. of diluted toxoid containing 3 Lf while those in the second group were given 1 cc. of fluid toxoid containing 40 Lf. Two weeks later blood samples were again taken. The data relating to this experiment are presented in Table V.

TABLE V

DIPHTHERIA ANTITOXIN RESPONSE TO RECALL DOSES OF 3 LF AND 40 LF OF FLUID TOXOID

Lf	Time	0.001 & >	0.01 & >	0.1 & >	1 & >	5 & >	10 & >	20 & >	40 & >	Total	Average Titre in Units
3	0	36	30	9	1	1	–	–	–	41	0.39
		88	73	22	2.4	2.4	–	–	–	100%	
	2 weeks	41	39	39	29	7	3	–	–	41	2.8
		100	95	95	71	17	7.3	–	–	100%	
40	0	36	25	15	1	–	–	–	–	38	0.28
		95	66	39	2.6	–	–	–	–	100%	
	2 weeks	38	38	36	32	20	12	4	1	38	8.6
		100	100	95	84	53	32	11	2.6	100%	

That both 3 and 40 Lf served as very effective stimuli is readily apparent. Whereas approximately 2.5 per cent in each group had 1 unit of antitoxin on the first bleeding, 71 and 84 per cent reached this level two weeks later. However, it is also apparent, as might have been expected, that 40 Lf produces a greater effect than 3 Lf. The difference is found to be statistically significant. This is true in spite of slightly weighting the experiment in favour of the 3 Lf group by placing all but one of those with a positive reaction test in this section.

This does not mean that 40 Lf should be considered as the dose of choice for recall purposes, for the question of reactions also influences its use. Among the 38 subjects receiving this dose of antigen there was only one with a positive (slight) reaction test. He and 10 others had local reactions to the subcutaneous injection, 4 of which were slight, 5 moderate and 2 severe. Of the 41 persons receiving 3 Lf of toxoid including 12 with positive reaction tests, there were 5 local reactions, 4 slight and 1 moderate. Four of these were positive to the reaction test. There were no general reactions in either group.

It seems reasonable to suggest that, in the light of this experience, the administration of 40 Lf of toxoid might have led to the occurrence of more severe reactions had the group not been screened for sensitivity to toxoid. On the other hand, the use of 3 Lf of toxoid produced no severe reactions in spite of its employment in 12 with positive sensitivity tests.

A further consideration is the rate of decrease in antitoxin in these two groups. It is planned to explore this matter, if possible, by tests at the end of one and three years.

Discussion

A study of the results reported here reveals that 91.3 per cent or 345 of 378 individuals responded to a recall dose. Omitting the 16 with no evidence of previous stimulation as gauged by absence of history of immunization, a titre of < 0.001 unit and failure to respond to the recall dose, 95.3 per cent responded. Since all but 38 received 4 Lf or less, the consistency of response must be considered very satisfactory. Omitting the 38 who received 40 Lf and the 16 lacking evidence of prior diphtheria experience, we find that 94.8 per cent responded, or 90.3 per cent if all the failures are included. It is apparent that a few who might have been expected to respond failed to do so. This may be accounted for by a recent prior stimulus, too small a dose of antigen, or other reasons. At any rate they constitute a small proportion only and already possess antitoxin, often in considerable amounts.

While it is highly important that the vast majority should show a response, the degree of this response is equally important. For all groups the number with 0.01 unit or greater before and after the recall dose was 217 and 349 respectively, or 57.4 and 91 per cent. Further, 75 per cent had 0.1 unit or greater after re-immunization as opposed to 24 per cent before. Of those given 4 Lf or less, 72.6 per cent reached a level of 0.1 unit of antitoxin or greater as opposed to 22.4 per cent at this level before the recall dose. One would presume that little diphtheria would occur in such groups.

That small doses of toxoid may serve as an effective secondary stimulus has been reported by other workers. Fraser (3) showed the effectiveness of 0.1 cc. of fluid toxoid as a recall dose in a group of 50 children, all of whom had < 0.02 and $8 < 0.001$ unit. All responded to > 0.05 and the majority to 0.5 unit. Volk and Bunney (4), from the results of a large-scale study, state that "The results seem to indicate that either 0.1, 0.5, or 1.0 ml. of fluid toxoid, or else 0.1, 0.5 or 1.0 ml. of alum precipitated toxoid, confers a satisfactory immunity in the majority of previously immunized children." Wilkie (5) used 0.1 cc. of fluid toxoid as a recall dose in 2791 school children who had received 3 doses of fluid toxoid five to ten years previously. Six weeks later only 2.83 per cent were still Schick positive. Such results are in conformity with those presented above for the groups receiving 2, 3 or 4 Lf where 97.5 per cent of the previously immunized showed a response.

As long ago as 1931, Fraser (6) noted the increase in antitoxin which may follow the administration of the Schick test and diluted toxoid control. This observation has been repeatedly confirmed. It might be suggested that the

Schick test and control would suffice for recall purposes, for example, in adults. That it is, however, likely to be less than satisfactory is indicated by our results. While all of 11 in Group III responded, 12 per cent of those with previous immunity in Group V and 18.5 per cent in Group VI failed to respond. Mather (7) reports somewhat similar results. In a group of 71 R.C.A.F. personnel who had relapsed to the Schick-positive state, he found, on re-testing 4 weeks later, that approximately two-thirds were Schick-negative and one-third still Schick-positive. All but 2 of those positive to the second Schick test became Schick-negative when given a larger dose of toxoid.

As yet we have obtained few data on the decrease of antitoxin over a prolonged period following the response to the recall dose. That a decrease does occur is well known and would be expected. Volk and Bunney (4) found the results in re-immunized children to parallel those following primary immunization. Groups I, II, III and IV illustrate this decrease over a three-year period. The rate of loss appears to go on about equally in all groups no matter what the recall dose, so that those who achieve high titres of antitoxin retain protective levels longer. This is, of course, a very important consideration. In order to profit in this way, a highly effective stimulus should be employed. However, it has been observed (4) that those with < 0.001 unit at the time of the recall dose respond less well than those with > 0.001 unit. Immunization programs might be so designed, therefore, to largely prevent this relapse to the < 0.001 unit state by giving the first recall dose within a relatively short period after the primary course, say at six months or one year. Mather (7) found the greatest loss of antitoxin and relapse to the Schick-positive state in adults to occur between six and twelve months after a primary course of 2 doses of alum precipitated toxoid given at a four-week interval. Approximately 25 per cent of his one-year group had become Schick-positive and had < 0.002 unit. Neubauer (8) has reviewed the literature relating to the Schick-relapse rate following primary immunization and notes reported rates of from 2 per cent at the end of one year to 34 per cent at the end of five years, depending partly on the incidence of diphtheria in the different environments. In our present study this loss of antitoxin was ascertainable in certain groups. Of the 50 children in Groups I, II, III and IV, 32 per cent had < 0.004 unit of antitoxin (the Schick level) six years after the primary course. In Group VII, 46 per cent had < 0.004 unit ten to eighteen years after the primary course and almost one-third had lost all detectable antitoxin (0.001 unit). The loss in Group VIII was less sharp, with only 8 per cent having < 0.004 unit at four to twelve years (average of six) after the primary course.

With these findings in mind, it would appear that the first recall dose should be given within six months of completion of primary immunization. Subsequent recall doses at three- or four-year intervals might be expected to maintain antitoxin at a satisfactory level on the average as indicated in Table I. With this routine relatively small recall doses would appear to suffice.

The occurrence of reactions to re-immunizing doses of toxoid is a determining factor in selection of dose to be employed. Either one must screen out reactors preliminary to giving a large dose or select a dose which will produce

no reactions of consequence. Since sensitivity to toxoid is to some extent a matter of age as well as individual variation, it is difficult, perhaps impossible, to arrive at any single solution. By screening Groups X and XI by means of the reaction test, 40 Lf resulted in no serious disability in those receiving this dose. On the other hand, 3 Lf produced no severe reactions in a group in which 30 per cent were positive to the reaction test. In contrast to these groups of school children, 2 Lf in young adults (Group IX) produced reactions in 15.7 per cent. These were mostly local and mild but 2 per cent had moderate general reactions requiring brief bed rest. Recently, 149 medical students were given 0.4 cc. of diluted toxoid containing 1 Lf. This group will form the subject of a later report, but the reactions encountered are of interest here. Local reactions were shown by 31.5 per cent of which 85 per cent were mild, 11 per cent moderate and 4 per cent, severe. There were 8 general reactions or 5.4 per cent. Of these 5 were slight and 3 moderate, the latter requiring brief bed rest. Reactions in this group were then approximately twice as frequent as in Group IX though 1 Lf was given instead of 2 Lf. This may be accounted for by the fact that the great majority of these students had been in the armed forces where many of them had received alum-precipitated toxoid. Mather (7) observed that approximately 25 per cent of Schick-positive adults gave positive skin reaction tests after receiving 2 doses of alum-precipitated toxoid.

In Wilkie's school experience (5) in 2791 children ranging in age from five to sixteen years who were given 0.1 cc. of fluid toxoid, 15.9 per cent showed either a local reaction or a local reaction plus general symptoms. Of 11 children with any generalized symptoms only 2 were ill enough to remain home from school.

It would appear, then, that for school populations 0.1 cc. of toxoid (4 Lf) could be given safely and with a minimum of discomfort in the case of children whose primary course of inoculations was fluid toxoid but that in adult groups this dose should be reduced or screening employed. Further exploration of this problem is required and planned. The use of less than 4 Lf requires the provision of suitably diluted toxoid. This might be preferable in any case since the administration of 0.1-cc. amounts is subject to somewhat greater inaccuracy than that of larger volumes.

Summary and Conclusions

The diphtheria antitoxin response following recall doses of antigen of different Lf value has been studied in 11 groups totalling 378 individuals.

Remarkably small amounts of diphtheria toxin or toxoid served to elicit an appreciable antitoxin response. This response varied with, though not in direct proportion to, the strength of stimulus employed.

In terms of consistency and degree of response, 4 Lf or less provided an antigenic stimulus in approximately 95 per cent of 340 persons and 72.6 per cent of this number attained an antitoxin level of 0.1 unit or greater as compared with 22.4 per cent with such titres before the recall dose.

Disturbing reactions were not encountered in school children given 3 Lf of fluid toxoid in spite of the inclusion among them of some with a demonstrated

skin sensitivity to dilute toxoid. On the other hand, doses of 1 and 2 Lf of fluid toxoid in young adults produced local reactions in up to one-third of the individuals injected. In addition, moderate general reactions occurred in approximately 2 per cent of such groups.

The antitoxin titre attained following the recall dose or the primary course of immunization decreases with the lapse of time, and a program of immunization should provide for recall doses at suitable intervals. Such recall doses should induce high titres of antitoxin in order that protective levels may still be present over a three- or four-year period in spite of the gradual loss.

Because of the early and marked loss of antitoxin by some individuals following the primary immunization and because those with residual detectable antitoxin appear to develop high titres more readily on re-stimulation, it is highly desirable that the first recall dose be given within six months to one year of the primary course. Subsequent doses at three- to four-year intervals should maintain protective levels of antitoxin in the vast majority of individuals.

For pre-school children where sensitivity to toxoid is not a problem, a recall dose of 20 or 40 Lf is desirable. In school populations, in order to avoid the necessity of preliminary reaction tests, 3 or 4 Lf of toxoid, because of its freedom from untoward effect and because of its proven efficacy in terms of antitoxin response, may be recommended as a suitable recall dose. A similar dose is effective for recall purposes in adults but, apart from emergencies, screening for reactors by means of the reaction test is desirable.

Acknowledgments

It is a pleasure to record our gratitude to Dr. D. T. Fraser and Dr. P. J. Moloney for their interest and assistance in this study. We are also indebted to Dr. C. W. Carr, Medical Officer of Health of Cookstown, for his generous co-operation in regard to school groups.

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The Standardization of Influenza Vaccine by Red Cell Agglutination and Antigenic Tests in Mice

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FOLLOWING the publication (Francis, Pearson, Salk and Brown, 1944) of the results obtained by the Commission on Influenza, Board for the Investigation and Control of Influenza and other Epidemic Diseases in the Army (U.S.), with an influenza vaccine made according to the method of Francis and Salk (1942), studies on the large-scale production of the vaccine have been carried out in these laboratories. The vaccine consists of equal volumes of influenza A and B suspensions, made from allantoic fluid by adsorption on embryonic chick red cells and elution into saline. Relevant details of the method of preparation were given in a previous paper by Hare, Curl and McClelland (1946).

Sixty lots of three to four litres have been made and all were tested by determining the agglutination titre for chick red cells of each component and the ability of the completed vaccine to protect mice against living virus. It is probable that the first of these tests indicates the total number of virus particles in the suspension and is therefore comparable to the standardization of a bacterial vaccine on the basis of bacterial counts. The second test was carried out to determine how antigenic for mice the vaccine may be.

METHODS

Preparation of the Vaccine

Equal volumes of influenza A and B red cell eluate vaccines (Francis and Salk, 1942) were pooled. The details of preparation are given in the paper by Hare, Curl and McClelland, but it may be mentioned that for the A component, the PR8 strain was used, for the B, Lee, and that the Weiss strain of influenza A used by Francis et al (1944) was not employed.

Determination of Red Cell Titre

The methods employed have been described in the paper by Hare, Curl and McClelland.

Antigenic Tests in Mice

For the PR8 component, two groups of eight mice were inoculated intraperitoneally with two doses a week apart of 0.5 cc. of vaccine diluted 1/5 in saline. In the case of Lee, two, and sometimes three, groups of mice were inoculated in the same manner with the exception that the vaccine was diluted 1/500. The reasons for employing more than one group of mice will be dealt with elsewhere in this paper. Seven days following the second dose

of vaccine, the mice were given a challenging dose of 0.05 cc. of virus suspension intranasally under ether anæsthesia. The challenging dose was an appropriate dilution of a 10 per cent suspension of lungs from mice which had been inoculated 48 hours previously with the suspension of frozen lungs used for seed.

Strains Used for the Infection of Mice

The influenza A virus used for infecting mice was derived from the strain PR8 F198, received from Dr. F. L. Horsfall in November, 1940. In these laboratories, the virus had been passaged in mice ten times and the resultant strain was designated PR8 F198 M10. The influenza B virus, FB75 Lee 8.147, used in these experiments was received from Dr. Thomas Francis, Jr., in October, 1944. Mouse lungs from the first and second passages of this material were used as seed throughout this work.

Seed Preparation

In the preparation of seed virus, the same procedure was followed for both the PR8 and Lee strains.

Forty-eight hours previous to the infection of immunized mice, a pair of frozen mouse lungs taken from the seed stock was ground up with alundum. From the calculated weight of lung tissue, a 10 per cent suspension in tryptic digest broth was made and centrifuged in an angle centrifuge at 2,000 r.p.m. for twenty minutes. The supernatant was removed and 0.05 cc. of this suspension inoculated into the required number of mice, usually six, and never fewer than four. All materials and apparatus used in these procedures were thoroughly chilled and the temperature of the suspension was never allowed to rise appreciably above 0°C.

When the challenge suspension was required 48 hours later, the infected mice were killed with chloroform, the lungs removed aseptically as speedily as possible, washed thoroughly with chilled saline and all mediasternal tissues dissected away. The subsequent procedures were the same as for the frozen lungs.

Determination of the 50 per cent Mortality End Point (LD50)

In order to determine the dilution of the infecting suspension at which 50 per cent of the mice will die (LD50), five groups of six mice of the same age as the immunized mice were inoculated with 0.05 cc. of dilutions of virus over a suitable range. The LD50 was calculated from the number of specific deaths in ten days by the method of Reed and Muench (1938).

Mice

The mice were all Swiss albinos from one dealer and at the start of the immunization tests weighed from twelve to sixteen grams.

Experimental Results

Red Cell Agglutination Titres

Owing to the fact that lots were made up by pooling many bottles of A (PR8) and B (Lee) vaccine, approximately equal volumes of A and B being

incorporated, it was not possible, except in a few cases in which preliminary pools were made, to determine directly the agglutination titre of each component. But in view of the fact that both the red cell titres and the volumes of each component of the 60 lots were known, the mean titre of each of the A and B components of the lots could be determined by a method for which we are indebted to our colleague, Mrs. Margaret Richardson. This method involves finding the geometric mean of the titres of all the bottles of influenza A or influenza B incorporated into the lot, and weighting the logarithm of each titre by comparative volume.

The results of these calculations for the 60 lots are given in Table I, which shows that the red cell titres of both components of 53 of the 60 lots were above 1,000. Of the seven lots that had titres below this figure, Lot 54 had a titre of 534 for its PR8 component and 1,459 for its Lee; Lot 48, 800 for PR8 and 906 for Lee. The remaining five had PR8 titres greater than 1,000, the Lee titres being for Lot 10, 800; Lot 24, 800, and Lot 55, 750.

TABLE I

NUMBER OF COMPONENTS OF LOTS WITHIN THE INDICATED RANGES OF RED CELL AGGLUTINATION TITRES

Red Cell Titre	Number of Lots	
	A Component	B Component
0 - 1,000	2	6
1,000 - 2,000	25	34
2,000 - 3,000	28	17
3,000 - 4,000	5	2
4,000 - 5,000	0	1
Total.....	60	60

In all the A components, the virus had been concentrated ten times. In regard to the B component, 9 of those in the 1,000 - 2,000 range, 9 in the 2,000 - 3,000, 2 in the 3,000 - 4,000 and 1 in the 4,000 - 5,000 were made with virus concentrated 13.3 times. One in the 1,000 - 2,000 range was made with virus concentrated twenty times, the remainder being concentrated ten times.

Antigenic Tests

In view of the fact that the Weiss strain of influenza A was not incorporated in the vaccine, the specifications laid down by the Division of Biologics Control, National Institute of Health, Washington, could not be met completely. Instead, the following specification was adopted. Each lot of vaccine, administered intraperitoneally in doses of 0.5 cc. a week apart, was required to protect 50 per cent of six or more mice against 10,000 LD50's of PR8 virus and 1,000 LD50's of Lee virus administered intranasally seven days after the last dose of vaccine. For the mice receiving PR8 virus, the vaccine was diluted one in five and for the mice receiving Lee virus, one in five hundred. This test is in all essentials that set up by the National Institute of Health, Washington, in their third revision, April 10, 1945, of their minimum require-

ments for influenza virus vaccine types A and B (refined and concentrated) but omitting the Weiss strain.

It may be stated forthwith that all of the lots made in these laboratories passed the test, the great majority with very little difficulty. The main problem lay in determining the dilution to employ for the challenging suspension, and, because of this difficulty, in four of the sixty lots repetitions were necessary, the number of LD50's administered in the first test being either too high or too low.

In part, this was due to the use of fresh suspensions for each antigenic test, which were not given a preliminary titration. Despite the fact that the technique for the preparation of virus suspensions was standardized as much as possible, the LD50's of successive preparations showed wide variation. This is brought out in Table II which gives the LD50's for all the suspen-

TABLE II

THE FIFTY PER CENT MORTALITY END POINT (LD50) OF THE UNDILUTED MOUSE LUNG SUSPENSIONS MADE OVER A PERIOD OF SIX MONTHS

Date	PR8 F198 M10	FB75 Lee 8.147 M2
Nov. 17	1,000,000	
" 23		1,000
Dec. 6		4,160
" 15	71,000	6,980
" 28	203,000	2,370
Jan. 5	698,000	19,900
" 12	349,000	31,600
" 23		48,800
" 29	441,000	44,100
Feb. 2	433,500	22,650
" 7	1,430,000	23,720
" 13	1,590,000	56,100
" 19	141,900	43,450
" 23	177,400	17,740
" 24		FB75 Lee 8.147 M2
Mar. 7	70,150	17,500
" 12	133,000	10,000
" 23	237,000	3,500
" 29		25,100
Apr. 4		10,000
" 9		31,600
May 3		10,000

sions made over a period of six months. It was therefore essential to employ at least two infecting dilutions of the PR8 suspension, and two, but preferably three, of the Lee virus in order to obtain one set of mice which would receive a number of LD50's greater than but not too much greater than that specified.

Number of LD50's of Virus against which Protection is Obtained

In setting up the tests, it was found advisable to make one infecting dose of virus very heavy and the other, it was hoped, somewhat nearer the minimum level of 10,000 LD50's of PR8 virus and 1,000 of Lee virus.

When the infecting suspension was in the neighbourhood of the standard laid down, the vaccine usually passed the test without difficulty, seldom more than one or two of the eight mice dying. It is unnecessary to give these results in detail. Of more interest perhaps is the behaviour of the mice receiving the larger doses of challenging suspension. This is brought out in Table III, in which the ability of the vaccine to protect the animals against the larger of the two doses of the virus employed in each antigenic test is shown. In regard to the A component, it can be seen that the vaccine, when diluted one in five, protected the mice against infecting doses as great as one hundred times the 10,000 LD50's of PR8 virus required.

With Lee virus, on the other hand, there is much less elasticity, no fewer than nine lots failing to pass when given doses of 10,000 LD50's or greater, which is only ten or more times that required. This is possibly due to the fact that the vaccine must be diluted one in five hundred and a minimum of 1,000 LD50's of Lee virus administered, whereas, in testing the PR8 component, the vaccine is only diluted one in five to protect against 10,000 LD50's. These lots passed, however, when challenged with other dilutions of Lee virus containing LD50 doses somewhat nearer 1,000.

TABLE III

ABILITY OF THE VACCINE TO PROTECT AGAINST THE HIGHER OF THE CHALLENGING DOSES OF VIRUS

Influenza A					Influenza B		
LD50's Administered	Number of Lots Vaccine Diluted				LD50's Administered	Number of Lots Vaccine Diluted	
	1/5		1/50			1/500	
	Pass	Fail	Pass	Fail		Pass	Fail
10,000 - 50,000	34	0	30	4	1,000 - 10,000	18	0
50,000 - 100,000	15	0	8	2	10,000 - 50,000	31	8
100,000 - 150,000	3	0	1	2	50,000 - 100,000	2	1
200,000 - 300,000	3	0	3	0			
300,000 - 400,000	3	0	3	0			
3,000,000 - 4,000,000	2	0	1	1			
Total.....	60	0	46	9		51	9

Pass implies that less than 50 per cent of the test mice died with characteristic lung lesions after receiving challenge virus of the LD50 specified.
Five lots were not tested at a dilution of 1/50.

Dilution of Vaccine to be employed for Immunization of Mice

In view of the high degree of protection obtained against influenza A when the vaccine was diluted one in five, all of the lots except five were also tested at a dilution of one in fifty. This further dilution of the vaccine, as might be expected, considerably impaired the ability of the immunized mice to withstand heavy doses of infecting suspension, no less than nine lots failing. This is also shown in Table III.

With influenza B, little or no protection was obtained with vaccine diluted one in five thousand instead of the one in five hundred employed. It is hardly necessary to give the details of these experiments in which three lots and five pools were tested, all failing at a dilution of one in five thousand.

Effect of Dilution of Vaccine on its Ability to Pass the Antigenic Test

As was shown in Table I, a large proportion of the vaccines had red cell titres greater than 1,000. Even those lots having one or both components with a titre less than 1,000 passed the antigenic test adopted. It therefore appeared to be of value to determine whether vaccines prepared in the usual manner and diluted with saline could, after such treatment, still pass the antigenic test. Two pools of PR8 and two of Lee were employed for this, the red cell titres of all of the four pools being 2,000 or higher. The pools were diluted according to the scheme in Tables IV and V, where the titres

TABLE IV

EFFECT OF DILUTION OF PR8 POOLS ON ABILITY TO PASS ANTIGENIC TEST

	Pool 80							
	Dilution							
	3/5	1/2	1/2.5	1/3	1/4	1/6	1/10	Saline Controls
Red Cell Titre	1,500	1,250	1,000	830	620	410	250	
Mice	1/8	0/8	1/8	1/7	0/7	0/8	1/8	7/8
	All mice received 45,400 LD50's							

	Pool 88					
	Dilution					
	3/5	1/2	2/5	3/10	1/5	Saline Controls
Red Cell Titre	1,200	1,000	800	600	400	
Mice	0/6	0/8	1/8	0/6	0/8	8/8
	All mice received 52,400 LD50's					

Numerator represents number of specific deaths in ten days and denominator number of mice infected.

of the diluted pools are also recorded. Each of these dilutions was then further diluted with an equal volume of saline to represent the missing A or B component. The "vaccines" made in this way were then tested for antigenic power in exactly the same way as were the regular vaccines. The results are given in Tables IV and V.

Insufficient mice were employed to give a very precise end-point but these results indicate clearly that in the case of influenza A the vaccine can be diluted as much as ten times, so that the red cell titre is as low as 250, and still remain capable of passing the test. The actual dilution at which the vaccine would fail to pass was not determined, but the fact remains that the vaccine is capable of very considerable degrees of dilution before it ceases to be antigenic in the tests employed.

In the case of influenza B, a better indication of the end-point was reached. In Pool 72, a dilution of 3/20 passed and 1/10 failed, and in Pool 77A, 4/11 passed and 3/11 failed. These experiments confirm the fact that the antigenic test is extremely lenient.

TABLE V

EFFECT OF DILUTION OF LEE POOLS ON ABILITY TO PASS ANTIGENIC TEST

	Pool 72							
	Dilution							
	3/10	1/4	1/5	3/20	1/10	1/20	1/40	Saline Controls
Red Cell Titre	1,200	1,000	800	600	400	200	100	
Mice	2/8	2/6	3/7	3/8	4/7	5/7	7/7	8/8
	All mice received 1,400 LD50's							
	Pool 77A							
	Dilution							
	6/11	5/11	4/11	3/11	2/11	1/11	1/22	Saline Controls
Red Cell Titre	1,200	1,000	800	600	400	200	100	
Mice	2/8	2/8	0/8	5/8	4/8	3/8	8/8	8/8
	All mice received 1,400 LD50's							

Numerator represents number of specific deaths in ten days and denominator number of mice infected.

DISCUSSION

The results of this work show that when influenza vaccine composed of A and B viruses is prepared by the method of Francis and Salk, it will pass reasonably severe antigenic tests. But the original specifications adopted by us were not in conformity, the standard for the Lee component being more severe than that adopted for the PR8. Two alternatives are possible: (1) to lower the standard for the Lee component, requiring a dilution of one in fifty

instead of one in five hundred or (2) to raise the standard of the A component, requiring a dilution of one in fifty instead of one in five.

If the former alternative were adopted, difficulties in respect to forecasting the dilution of challenging virus to use would be eliminated. If the latter were adopted, more mice would be required to obtain challenging suspensions close to the minimum required; or, possibly, frozen, previously titrated suspensions would have to be employed. This expedient is open to question, for there is a definite tendency to alteration in titre when the mouse-lung suspensions are kept for any time frozen in the dry-ice refrigerator.

Experiments in which pools were diluted with increasing amounts of saline and then tested antigenically would suggest that the ten times concentrate made by the red cell elution method can usually be diluted quite considerably with saline and still pass the antigenic test. It is, however, uncertain even yet whether the undiluted material is fully protective for human beings. For this reason, the adoption of an antigenic test of low stringency may have obvious dangers if mass immunization is a possibility.

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THE CONTROL OF DIPHTHERIA

CHARLES J. O. HASTINGS, for many years medical officer of health of Toronto, used to say, even before Ramon's discovery of toxoid, "Every death from diphtheria demands a coroner's inquest." To-day, the truth of his words bears even greater weight since we now have a safe and sure means of controlling that scourge of childhood which only twenty years ago, in Canada, ranked second as a cause of death in the 2 - 14 age group in which it accounted for one in seven deaths from all causes. Is there really any sense in pegging away at the tiresome old topic? Is there really any purpose in reiterating the slogans, "Toxoid Prevents Diphtheria", "Have Your Child Toxoided" and so on? Is not diphtheria already under control? Was not Canada used on the bill-boards in England during their immunization campaign as an example of what can be done, with the challenge, "If Canada can do it, why can't we?"

In the January issue of the American Journal of Public Health, Gaylord Anderson reviews the trends in diphtheria in foreign countries as contrasted with the United States. A sharp increase in rates marked the war period along with the appearance of a more severe type of the disease in certain countries. He points out that Eire experienced a sharp increase whereas England and Wales, in spite of the congestion of the population and disruption of normal living conditions, enjoyed a decline to the lowest rates ever recorded and to levels comparable with those in the United States during the same period. England, facing the risk of increasing diphtheria, pursued a vigorous campaign of immunization; Eire did not. England was the only part of north-western Europe with a significant decrease. Anderson says: "May it not have been more than mere coincidence that it was also the only country that increased its immunization program to a point comparable with that of the United States and Canada?" He goes on to say that the data strongly suggest that immunization is effective against whatever strains may have been prevalent, an opinion which we strongly endorse.

Diphtheria toxoid was made available in Canada in 1927 under the prevail-

ing policy of free distribution by provincial departments of health. With the possible exception of France, Canada was the first country to supply diphtheria toxoid on a nation-wide basis. Within a few years of its introduction, more toxoid was used in Canada per unit of population than in any other country. Early field studies (1926-1930) established its effectiveness beyond all shadow of doubt. Following the procedure of immunization in use at that time, diphtheria was reduced by ninety per cent in Toronto school children as compared with the rate in unimmunized controls. The sustained record in the cities of Brantford, Hamilton and Toronto became a byword. With the wider use of toxoid, the diphtheria rate fell in Canada and in the United States to an all-time low, which situation has been reached in England some ten years later.

To-day Canada is no longer in first place in the race for diphtheria control; after taking the lead in 1932 and increasing it for some years, Canada dropped back and is now trailing. The rates for 1944, the last available figures for comparison, are: the United States, 0.9, England and Wales, 2.3, and Canada 2.6 per 100,000. The fact that, unfortunately, human lives are at stake should add seriousness and zest to the friendly rivalry of this international race.

The article by Wishart in this issue stresses two of the most important factors in the control of diphtheria. It has long been known that the response to toxoid and the loss of antitoxin are subject to very wide individual variation. Both of these factors may be countered by giving the "dose de rappel" of Ramon (or more commonly designated as the "booster" or recall dose) in suitable quantity and at appropriate intervals. In his detailed study, Wishart has explored particularly the effectiveness of small doses and the duration of antitoxic immunity conferred thereby.

The secondary stimulus is the really important factor in conferring and maintaining a safe immunity in both diphtheria and tetanus. There must first be established a basic immunity through an effective primary stimulus. Toxoid of 40 Lf value given in three doses of 1 cc. each will effectively accomplish this if spaced about one month apart. A secondary stimulus or booster dose is essential, and without it, in our view, the immunization procedure should very emphatically not be considered completed. When this reinforcing dose is best given may still be a matter of opinion. It is known to be effective at three months, at six months, and at one year after the third dose. It becomes perhaps an administrative problem which of these intervals best suits the local conditions. It is, of course, advantageous to raise the antitoxin titre to as high level as possible as soon as possible. Thereafter, the level of antitoxin may be kept high with suitably spaced small stimuli.

Essentially, the control of diphtheria rests upon the simple principles of producing the most effective degree of active immunity in the greatest number of persons in the least time and maintaining that immunity indefinitely. Administratively, this looks like, and perhaps is, a formidable task. It would be disastrous, however, if, through apathy on the part of the family physician or on the part of the public or through administrative fumbling, the gains we have made should not be maintained and extended. One effective means toward the control of diphtheria, in the meantime, would be to accept Hastings' advice and thus assess more realistically the factors concerned in the inadequacy of our methods.

The British Citizen and His Nurse

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IN 1948 Great Britain proposes to launch her National Health Service, one of the most ambitious social schemes in history. It will not be a free service. Quite expensive stamps must be paid for weekly, and duly affixed. But Great Britain began stamp-licking for health over thirty-five years ago, and the present scheme is only a vast elaboration of the old, but partial, health insurance introduced in 1911 by the then Chancellor of the Exchequer, Mr. Lloyd George—not without considerable demur from what came to be known as the "panel" doctors, and with many a gibe at stamp-licking in general.

The present National Health Service, which embraces everyone, is nevertheless only one part of a still more comprehensive scheme to even out the ups and downs of life—unemployment, industrial injury, sickness, old age, and so forth; and the cost is to be shared by the State, the local government authorities, the people and their employers. It is said that the best yardstick of a nation's standards of civilisation is the care it takes of its weaker members. If this is so, then Great Britain has no reason to be ashamed of her record. Whether incentive and ambition will be lost in the process remains to be seen. Most people over here think not.

In future, perhaps by April, 1948, *everybody* will have a claim on our health service. The quality will be the same for everyone—unless they insist on luxuries—and that quality will be as good as the nation can make it. People can consult a doctor, be admitted to hospital, be helped to regain fitness or remain fit, and be nursed when ill. Obviously, with everyone claiming these benefits as a right, it is very doubtful at first whether there will be enough facilities to go round. We know there are not enough dentists, for instance, and that mothers and children will have to come first. Hospital buildings and beds are still inadequate, and, even where they exist, wards are being closed because of that world-wide problem—the shortage of nurses.

When the plan for a national health service was first drafted, an adequate supply of nurses was more or less taken for granted—until the nurses themselves pointed out that things were not quite so simple, and that without some hard thinking, a reforming spirit and a good deal of consultation and mutual cooperation between nurses and Government, our health service would fall to the ground. A large staff of well-trained nurses and auxiliaries is essential if the structure is to fulfil expectations.

Fortunately the relations between the nursing profession and our Government are good; the consultative approach is well established. Our nurses are used to negotiating on a national scale on such matters as scales of salary and conditions of service, each national nursing organization having representation according to weight of membership. For instance, as the Royal College of Nursing, with which I am concerned, is the largest organisation, it has the largest allocation of seats. Moreover, our College, which is a "protective" and negotiating as well as an educational body, is not only in constant touch with Government departments, but, being affiliated to some forty national organisations with kindred interests, is also in touch with public opinion.

Throughout the controversies which the introduction of this measure has provoked, the Royal College of Nursing has led the nurses in maintaining that the national health service is primarily designed for the good of the community, and not primarily for the good of those who will carry out its provisions. We nurses over here have as our target a complete nursing service for every citizen in every walk of life, and though we know this target cannot be achieved just yet, we know that we ourselves can do most to bring it about.

For those who do not know the main outline of our national health plan, and for the purposes of this article, it can be briefly summarised as follows. The service will be administered through three main but intercommunicating channels—a hospital and consultant service, a full and varied clinic service, and a family doctor service. All these services will be under the ultimate control of the Minister of Health, who will also be advised by a council made up of the various professional interests (including nursing) and their appropriate committees. The plan on paper seems sound enough. Whether it will become a real live entity or be strangled with red tape depends largely on the flexibility of the Government officials concerned.

The hospitals, apart from the famous "teaching" hospitals, for which special provision is made, will be organised on a regional basis, each region being centred on a university medical school. The existing "voluntary" hospitals will henceforth, like the rate-aided hospitals of the local authorities, be state-owned, and our mental hospitals, which have tended to be somewhat isolated communities, will be welded into the local plan.

The co-ordination of hospital services should make for a better and broader training of our nurses, and, we hope, a better distribution of available candidates for training. The shortage of nurses is world-wide, and, though some of the causes are special to this country, the general picture is much the same elsewhere—an ageing population, in which a diminishing number of young people must cater for an increasing number of the elderly; the many rival careers open to women; the increasing complexity of medical treatment and the absolute increase in nursing hours spent on individual patients; the effort to shorten the nurses' working day; wastage among trainees, caused partly by the tendency in these difficult days to look on student nurses as a cheap source of labour, and, among the less popular training schools, to accept applicants irrespective of their suitability in order to maintain the service; and, lastly, overwork among trainees due to the acute shortage of domestic help.

Great Britain is watching with interest the psychological and other selection tests for nurse candidates which have been adopted by certain nursing schools across the Atlantic. Such tests are extensively used by our Army, Navy and Air Force, and some hospitals are using them experimentally. During the war the educational standard demanded of nurse candidates by our State examining body, the General Nursing Council, had to be waived, and the Council's decision to introduce even the more modern tests of intelligence and suitability is hotly contested by hospital authorities. These authorities fear that such a step will have disastrous effects on recruitment, and will overlook the "born" nurse, who may be better with her hands than with her head.

We nurses maintain that it is useless to accept as student nurses candidates who, according to the tests, have little chance of making good, and that they should be directed from the outset to a simpler training—for example as assistant (or, as you would say, "practical") nurses, working under supervision, or as ward and departmental orderlies. Far from jeopardising recruitment—unless it be of unsuitable candidates—this would obviate wastage and disillusionment from the start.

The proper selection of candidates must, however, go hand in hand with a complete overhaul of our systems of hospital staffing and nurse education

and training. We know that we can only recruit a certain percentage of the intelligent womanhood of the country, but, once having recruited this percentage, we must make each candidate feel that she is a student training for a *qualified profession*; and when we have trained her, we must not fritter away her skill in tasks which can be performed by auxiliaries. We emphasise that no nurse should consider it beneath her to perform the smallest service for the comfort of her patients, but it is only common sense, in these days of specialisation and delegation, to make the most of skilled but limited personnel. An alternative suggestion, which is meeting with considerable support, advocates a two-year basic course in pure bedside nursing for all candidates, followed, for those who aspire to posts of leadership and responsibility, by a course of a much higher standard. There is, perhaps, more in common between these two points of view than might at first appear. Both aim at a large increase in the number of nurses trained to carry out the simpler nursing duties, and a greater selectivity (with, at first, inevitable reduction) among those attempting the more advanced training.

There is, of course, very little likelihood that the hospitals will at first be able to meet all the demands made on them, and many patients will still have to be nursed at home. This will bring them into the second big group of services into which the scheme is divided—the clinic services. Such services—health visiting, maternity and child welfare, and so on—being of a more intimate nature, will be run on much the same lines as hitherto, that is, under the auspices of the local authorities—the county councils and big towns.

Nursing in the home will be one of these services, and the local authorities will either run their own service or pay one of the present voluntary associations to do it for them. In any case all domiciliary nurses will have the same training. So far our (voluntary) district nursing associations have only provided a visiting service, chiefly among people of very limited means, and have left the household to carry on as best they could between visits. Those who needed (and could afford) a resident service have always employed a private-duty nurse. But though the war has improved the position of the lower income group, it has left many of us very much poorer, and it is doubtful whether the middle classes will have either the means or the inclination to pay for private-duty nursing once they become contributors under the scheme. If they cannot enter hospital, they will expect full-time nursing in the home as a right. Therefore, since everyone, rich and poor, is to be treated alike, the new domiciliary nursing service must be considerably extended, and must absorb—by what means is still under discussion—those existing private-duty nurses whose prospects of regular employment under the new regime will almost vanish.

The most important innovation in the local clinic service is the duty laid on local authorities to set up "health centres," where clinic services can be carried on, and which can be used as joint surgeries by groups of family doctors engaged in the service. The centres will not be built to one set pattern; they will develop to meet local needs. But from the point of view of the public, it should be helpful to find a number of related services, medical, dental and nursing (both public health and domiciliary) housed in modern, publicly owned premises, which, it is hoped, will also take their place as centres of health education. We nurses feel, however, that one link is missing from this chain of clinic services: industrial health is regarded as outside the scope of the present Act, and we consider that it is a grave mistake to separate such an important branch of social and preventive medicine from the service as a whole. We maintain that the smaller factories could make good use of the health centres for the examination of new entrants and the carrying out of minor treatments, and that continuity and co-operation with other services would be economic both of time and money. It is possible that

this omission may be made good at a later stage.

Such, in brief, is the outline of the British health plan as it affects the British citizen and his nurse. The citizen will have to pay his share of the scheme, and at first he may not get all he thinks due to him in return. His nurse is well aware of these threatened shortcomings, and is tackling some formidable problems in her efforts to overcome them. It is some consolation to know that she is not alone in her troubles—the problems are world-wide. And it has occurred to me since my recent travels in Canada and the United States, and my talks with nurse leaders from South Africa and other parts of the British Commonwealth, that since, in this period of transition, we appear to have so many difficulties in common, we English-speaking nurses should now meet and examine the situation together. Then, after taking council, we could go forward again on a common front, to the benefit of the citizens of East and West alike.

BOOKS

The Modern Attack on Tuberculosis. By Henry D. Chadwick, M.D., and Alton S. Pope, M.D. 2nd ed. New York: The Commonwealth Fund, 1946. 134 pp. $1.00.

THE REVISED EDITION of *The Modern Attack on Tuberculosis* should be in the library of every physician engaged in public health or tuberculosis control. It contains a wealth of information on the epidemiological aspects of the disease with related statistical information not easily obtained. The influence of age, economic and living conditions, types of work and race is discussed.

The problem of tuberculosis control among staff of general hospitals and mental hospitals is considered and the suggestions given to protect the staffs of such institutions are very timely.

Stress is placed on the importance of the removal of the source of infection from the home or industry from the public health view. It is refreshing to read that the authors place segregation of infectious cases in sanatoria as a most important factor in the decline in the incidence and mortality from this disease in more recent years.

Case finding is discussed in detail as to methods and selected groups but no specific mention is made regarding community mass surveys Community surveys uncover many unknown cases of tuberculosis that would be missed if the examinations had been confined to selected individuals such as industrial groups. It is the reviewer's belief that employers and employees will avail themselves of the opportunity given for X-ray examination in community surveys by presenting themselves at the clinic, often with their families.

The proper organization of a community approach to the eradication of tuberculosis is well described and the need of adequate diagnostic facilities emphasized. The chapter entitled "A Community Campaign" is most complete and the value of proper records is shown to be essential.

This book gives a clear presentation of the subject and it is hoped that it will be used as a reference by health officers and public health nurses.

G. C. Brink

Water Bacteriology. By Samuel C. Prescott, C.-E. A. Winslow, and M. H. McCrady. 6th ed. New York: John Wiley & Sons, Inc., 1946. 368 pp. $4.50.

THE SIXTH EDITION of *Water Bacteriology* takes a relativistic view of those microorganisms introduced into water from extraneous sources. It is a view relative to the sanitary significance of those organisms and considers the multitudinal factors involved in the source, introduction, maintenance or growth, and detection of these. The fluctuations in bacterial populations in water are discussed and the factors considered. In regard to samples for examination, the question of representation of the water in question is brought under sharp focus. The authors stress the difficulties of water examination by saying ". . . the factors involved are so complex and the evidence necessary so indirect, that the process of reasoning much more resembles a doc-

tor's diagnosis than an engineering test."

This being the problem, they feel no test is as yet altogether satisfactory, but those tests for organisms of the coliform group are the most satisfactory to date. Of these organisms, they say: "Organisms of the coliform group find in the intestine of the higher invertebrates an environment better suited to their growth and multiplication than any other which occurs in nature." It is . . . "almost certain that the only way in which large numbers of these organisms gain access to natural waters is by pollution with domestic, industrial, and agricultural wastes of human life. If pollution has been recent, coliform organisms will be found in comparative abundance. If pollution has been remote, the number of coliforms will be small, since there is good evidence that the majority of intestinal bacteria die out in water. If derived from cereals or the intestines of wild animals, the number will be insignificant except perhaps where the water receives refuse from grist-mills, tanneries, dairies, or lactic-acid factories." The authors consider that there is no simple, unvaried answer to the problem of the sanitary significance of different types of coliform organisms and conclude "The ratio of number of *E.coli* to that of other coliforms in a water cannot be relied upon as an indication of its sanitary quality. Although the presence of *E.coli* in water may be considered in general to be more indicative of recent and dangerous pollution than is the presence of other coliforms, this generality is so subject to exception that its usefulness in the practical interpretation of coliform results is, save in a few particular instances, problematical."

Suggested tests utilizing the demonstration of streptococci and anaerobic organisms are appraised and the opinion given is that for use with water of good quality, the demonstration of these organisms constitutes a less delicate test than the detection of the presence of coliforms. The authors outline and discuss three phases of water examination, the 20°C. plate count related to the amount of organic material in the water in question, the 37°C. count related to the microorganisms which thrive at body temperature, and the coliform test related to organisms coming from the gastro-intestinal tract of vertebrates. For the latter, McCrady, in order to determine the usual practice in reading enrichment tubes, obtained by questionnaire the opinions of twenty-five bacteriologists. The majority agreed that the presence of gas, whatever the amount in forty-eight hours, was of sanitary significance. Because of the complexities involved, the authors are wary of complacency over tests in vogue and feel improvement of tests will come from trial-and-error methods. Here they emphasize the necessity of being aware of many factors, and advocate the use of a mixed bacterial population when evaluating tests.

All those concerned with sanitation and water supplies will find much of interest in this indispensable volume. For a technical subject the treatment is quite refreshing. If any criticism is justified, it might well relate to the great number of references dealt with. By many this would be considered a virtue and the-better-than fifty pages of bibliography a treasure. Two final chapters, one dealing with sewage and the other with shellfish problems, round out the value of this volume.

J. R. Parker

Rheumatic Fever. By Herbert Yahraes. Public Affairs Pamphlet No. 126. Issued by the Public Affairs Committee Incorporated, 22 East 38th Street, New York, and prepared in conjunction with the American Council on Rheumatic Fever of the American Heart Association, Inc. 31 pp. 10c.

THIS IS undoubtedly the best summary on rheumatic fever that is available for the layman, but it is equally useful for the physician. It sets out, in terms that can be readily understood, an outline of the causes of rheumatic fever, its treatment and prognosis. It also stimulates the reader to be interested in the public health aspects and to do what he can in a community program to deal with this serious disease.

The chart in the middle of the pamphlet which shows the various organizations that need to be co-ordinated in order to develop a suitable program is very good and should catch the eye of everyone. The author has also arranged an entertaining illustration depicting the prognosis based on the work of Dr. T. Duckett Jones. Those of us who are fishermen will be glad to see that we can pursue our hobby even if we develop rheumatic heart disease.

This pamphlet should be put in the hands of every parent with a child who has rheumatic fever or heart disease, and should be widely distributed about the community to all sections and organizations who might be interested in treating, preventing and investigating the disease.

John D. Keith

Table of Food Values Recommended for Use in Canada. Ottawa: Nutrition Division, Department of National Health and Welware, 1946. 183 pp.

THIS IS the first comprehensive set of tables of food composition published in Canada. While based primarily on the table issued jointly by the U.S. National Research Council and by the Bureau of Human Nutrition and Home Economics of the U.S. Department of Agriculture, it contains a great deal of Canadian data. The preparation of the Canadian table was originated by the Committee on Food Analysis of the Canadian Council on Nutrition. There has been an urgent need in Canada for tables of food composition and this publication meets the need admirably. Particular attention should be directed to the format. The loose-leaf arrangement and the page style make the table convenient to use. The primary U.S. data are perhaps the most accurate available at present. The inclusion of Canadian figures, e.g., on Canada Approved bread, adds to the usefulness of the publication. It is to be hoped that this table will be generally used in Canada, not only because of its worth, but to give uniformity to discussions of food composition in this country. It should be available to, and used by, all public health nutritionists in Canada.

E. W. McHenry

ABSTRACTS

The Protective Effect of Vaccination Against Epidemic Influenza B in an Industrial Plant

THIS STUDY was conducted in a plant employing 4,646 persons of whom 366 were given 1 cc. of combined concentrated influenza A and B vaccine. The experiment was begun fortunately just at the start of an epidemic of influenza B. The vaccinated and control groups, apart from size, were closely comparable except that those most susceptible to repeated respiratory infections probably volunteered more readily for vaccination.

Among the 366 vaccinated persons there were 13 cases of influenza, an incidence of 3.55 per cent. However, only 7 of these had received the vaccine more than 7 days before the onset of their illness, or early enough to give reasonable time for antibody development. Thus the incidence could be regarded as 1.94 per cent.

Of the 4,280 unvaccinated controls, 352 developed influenza, an incidence of 8.23 per cent. Thus the incidence was 2.3 times as great among the unvaccinated or 4.25 times as great as in the group vaccinated early enough to allow antibody response. Loss of time due to sickness was 4.4 times as great in the unvaccinated group as in the group vaccinated in time for antibody response.

The results would seem to indicate a definite protective effect against epidemic influenza B. These findings are in essential agreement with those reported by Francis, Salk and Brace from a study conducted in army groups during the same epidemic.

W. D. Norwood and R. R. Sachs, Indust. Med., 1947, **16**: 1.

Treatment of Pediculosis Capitis with D.D.T. Emulsion

DURING AN EIGHTEEN-MONTH period, 400 patients were treated for pediculosis with D.D.T. without ill effect. At first, the drug was used as a 4 per cent solution in liquid paraffin, latterly as a 2 per cent emulsion with naphtha 15 per cent, emulsifying agent 5 per cent, and water 78 per cent. The emulsion was worked thoroughly into the hair and scalp with a two-inch paint-brush. Patients were then directed to wash the hair the following day and return for removal of nits with a nit-comb. Usually one combing sufficed, but occasionally two or more were required in the presence of heavy infestation.

Since lice were known to be killed in approximately half an hour, washing of the hair one hour after treatment followed by immediate combing for nits was tried and appeared to be as successful as the longer process.

Only one reaction was encountered in the series. This consisted of inflammation and swelling of the nose, forehead and eyelids in a woman with extensive impetigo in addition to pediculosis. The reaction was of brief duration. In cases with a secondarily infected scalp, the pediculi were first destroyed and then the infection treated.

A. D. Frazer, Brit. M. J., 1946, August 24, p. 263.